

SARCOMA OF THE BREAST

A Study of Malignant Mesenchymal Neoplasia

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Summary

Mammary sarcoma is a very rare tumour and few large series have been reported - most are reviews of reported cases. The cases available for my own study, collected over many years, are exceptional in their number, over 100, and in their varied structure. This thesis is an account of the histological study of these cases. It demonstrates the manner in which the normal progeny of primitive mesenchyme have their counterpart in the malignant tumours which arise and that, in any given tumour, a variety of cell types is frequently observed.

In many cases, it has been possible to trace the transition of the benign precursor, the simple fibroadenoma, to the frankly malignant sarcoma, a feature more readily demonstrated in cases where whole breast sections were available. The variety of metaplastic development was a surprising finding and is amply illustrated in the cases described.

In rare cases, the malignant change in the fibroadenoma was found in the epithelial component. A few cases in which neoplastic transformation occurred in both elements are also described. Limited comparison with similar growth in other tissues or organs, is also included.

Where possible, the clinical and pathological findings are correlated.

INTRODUCTION

Sarcoma of the breast is a rare tumour. During 12 years of routine reporting at the Research Laboratory of the Royal College of Physicians of Edinburgh, 16 sarcomas of various types were encountered among 1,680 malignant mammary tumours examined. This frequency agrees with a general finding of about 1 per cent in recorded series (Sailer, 1937; Curran and Dodge, 1962). Earlier figures vary greatly. Some were higher because malignant tumours which were not obviously carcinomatous were diagnosed as sarcoma, giving a frequency even as high as 6 to 9 per cent (Geist and Wilensky, 1915); others were lower (Schreiner and Thibaudeau, 1932; Adair and Hermann, 1946) because incidence was sometimes based on all breast lesions or on all breast tumours. The most satisfactory index of incidence is a comparison of sarcomas and carcinomas in general reporting material.

Material

This study is based on an unusually large series of over 100 personally studied mammary sarcomas. They have accumulated over many years and having been received from many sources in this country and elsewhere, the numbers have no statistical significance. The great majority have been sent by pathologists because of my special interest in mammary pathology. The material initially available for study included about 80 cases which had been regarded as definite or possible cases of mammary sarcoma; critical examination excluded 30 of these. During subsequent years 50 more cases were referred or found in routine reporting material and these have been added to my original series. In some cases, complete operation material was available, with adequate clinical data and a later follow-up; in others, only biopsy material or prepared stained sections were sent. In the study of a rare and often debatable tumour, such limitations are necessarily but unavoidably restrictive. A number of cases were prepared as whole-breast or whole-tumour sections and were particularly instructive. The wash drawings, done by myself during the war, served as a substitute, to some extent, for whole-breast sections in some cases, in conjunction with many small slides.

Staining Methods

In addition to routine staining with haematoxylin and eosin, various stains such as

Masson's trichrome, van Gieson's stain, Lendrum's reticulin stain, periodic acid-Schiff (P.A.S.), Scharlach R and occasionally other stains were used if considered necessary for unusual histological structure.

A preliminary survey brought out several points:

1. Very few of the cases which were histologically acceptable as sarcomas, had been diagnosed clinically as such on initial examination, even if advanced and ulcerated. If early, they simulated fibroadenoma; if late, advanced carcinoma of cystic or medullary type or an inflammatory condition or if very large, were diagnosed as "cystosarcoma phyllodes" or Brodie's "sero-cystic disease". Some were described clinically as "malignant" without further definition.
2. In no case of this series was there histologically proven axillary involvement, an important diagnostic point.
3. On transection the macroscopical appearances varied greatly. Some tumours showed the bulky, nodular, vascular and occasionally ulcerated growth of variable structure as in an advanced lesion. Others simulated a benign fibroadenoma even if the subsequent histological examination proved active malignancy. All intermediate grades were encountered.

The great majority were single tumours but in a few cases multiple sarcomas were found in the corpus mammae. The rarest occurrence was the finding of two malignant tumours of different type which proved to be coincidental carcinoma and sarcoma.

4. The most important point which emerged from a preliminary survey of the series was the necessity of an attempt to trace the histogenesis and evolution of the sarcoma. This necessitated adequate material for study and differential staining.

This tracing of development from the most frequent precursor, a fibroadenoma, explains many of the anatomical and histological features of mammary sarcomas. It also supplies criteria for diagnosis and in many cases also provides an answer to such questions as (a) is this tumour a sarcoma or an atypical carcinoma?; (b) if sarcoma, is it primarily mammary, i.e. derived from the corpus mammae and not from some adjacent tissue such as overlying dermis, surrounding fat or even pectoral muscle?; (c) is it possibly metastatic from some cryptic primary source, e.g. a lymphoid neoplasm or a non-pigmented melanoma

of spindle-cell structure?; (d) if mesenchymal and primary in the mamma, is it really malignant, with the possibility of forming metastases? A later history or autopsy examination would have answered most of these questions, but this information was rarely available in the large series studied because of the many sources of the material sent me, the movement of population in Britain during the wars and the fact that the great majority of patients with mammary cancer do not die in hospital. The presence of metastases, when known, is therefore usually an earlier finding by radiography or is clinically evident.

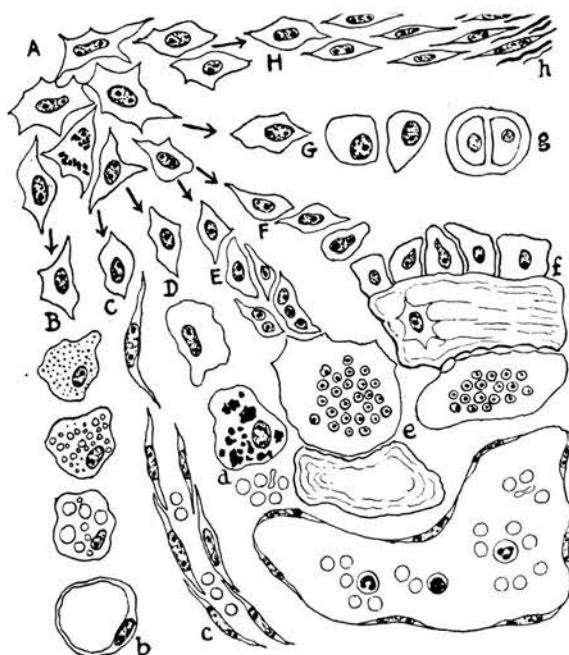
5. Mammary sarcomas are peculiarly prone to metaplastic change, resulting in the formation of tumours exhibiting bone, cartilage or fat. In this study these variants are described as separate groups.

6. A majority of cases have a characteristic history of longstanding tumour which has shown little change for many years followed in middle age by sudden rapid growth.

CLASSIFICATION

So varied is the structure of mammary sarcomas, even in sections from a single case, that any rigid classification is misleading. The dominant tissue is, however, usually recognisable and by this the tumours can be broadly identified. These tissue types correspond to the main lines of differentiation of the primitive mesenchyme cell as shown in the diagram below.

| | | |
|----------------|---|------------------|
| Fibroblast | - | Fibrosarcoma |
| Osteoblast | - | Osteosarcoma |
| Chondroblast | - | Chondrosarcoma |
| Lipoblast | - | Liposarcoma |
| Haemangioblast | - | Haemangiosarcoma |



- A. Primitive mesenchyme
- b. Differentiation to lipoblast
- c. " " angioblast
- d. " " macrophage
- e. " " osteoclast
- f. " " osteoblast
- g. " " chondroblast
- h. " " fibroblast

Mammary sarcomas which show all these derivatives are illustrated here.

Differentiation to other cell types is not indicated in this diagram as no examples of tumours formed from them were available for study. The lympho-reticular tumours are excluded as mentioned later. Myeloid blood cell formation has been found as bone marrow tissue only in canine tumours (fig. 383). Sarcomas with metaplasia to striped or smooth muscle are very rare in the breast. Single examples of rhabdomyosarcoma

have been recorded by Sailer (1937) and Winston Evans (1953); Sirsat (1959) reported a mammary tumour with varied stromal metaplasia, including smooth muscle. The "myoadenoma" (Figs. 372 & 373), a very large human tumour which showed nuclear palisading, some mitotic activity and apparent early osteoid tissue but no evidence of genesis from the media of arterioles may be a human example of tumour derivation from myoepithelium and be a leiomyosarcoma but no further data or differential staining was available.

Tumours are also found in which both epithelial and mesenchymal elements participate.

Carcinomatous fibroadenoma

Carcinosarcoma

In this study the cases examined were grouped partly on the pathological basis as above and also on age and sex, since these examples illustrated special features.

Certain additional cases of exceptional character or in which precise diagnosis remains doubtful are grouped separately.

The appended table illustrates the grouping employed and the cases in each group.

CLASSIFICATION

| <u>Type</u> | <u>Cases</u> |
|-------------------------------------------------------------|-----------------|
| Fibrosarcoma | 1 - 33 |
| Osteo- and Chondrosarcoma | 34 - 51 |
| Liposarcoma | 52 - 59 |
| Haemangiosarcoma | 60 - 69 |
| <u>Special Groups:</u> | |
| Tumours in young age group - female | 70 - 73 |
| Tumours in male patients | 74 - 77 |
| Evolution of Sarcoma | Figs. 235 - 262 |
| <u>Tumours with both mesenchymal and epithelial tissues</u> | |
| Carcinomatous fibroadenoma | 78 - 86 |
| Carcino-sarcoma | 87 - 94 |
| Rare and doubtful | 95 - 109 |

FIBROSARCOMA

Cases 1 - 33. Figs. 1 - 75.

Fibrosarcoma

The fibrosarcomas form the largest group in this series of malignant mesenchymal tumours of the breast, a predominance of type supported by the 70 per cent incidence in various recorded series. With the exception of the few rarer types shown later, in this group of tumours, the initial abnormal activity is seen in the formation of a primitive very vascular myxoid tissue. The site of this malignant change is usually demonstrated in the subepithelial zone of a pre-existing fibroadenoma, an activity which may, in whole or in part, have eliminated the epithelial component when the tumour is examined, though the polypoidal stromal pattern may still be recognisable. In more advanced cases, the myxoid tissue is gradually replaced by a more cellular tissue.

By some pathologists, the presence of myxoid tissue has been regarded as a degeneration. My studies demonstrate its ominous significance as evidence of the emergence of an active primitive tissue (Maximow 1926, Ewing 1935, Thibaudeau et al. 1935) which may appear in recurrent as well as in primary sarcomatous tumours. This vascular myxoid change is usually ill-defined and may be extensive and mingled with more cellular growth. In the first case illustrated here, multiple cellular fibroblastic patches were defined by contrast with a generalised myxoid change.

The commoner mammary sarcomas are usually divided into 2 main groups, adenofibrosarcomas and pure fibrosarcomas, according to whether glandular tissue is or is not present in the tumour (Cheate and Cutler 1931). My material, however, suggests that this classification is more a difference between an earlier and a later stage of fibroblastic activity than a difference of tumour type, though in adjacent areas of the purely fibroblastic tumours a few scattered surviving ducts may be found. This finding becomes progressively less frequent at the advanced stage of tumour growth.

The malignant fibroblasts may undergo metaplasia resulting in the formation of bone, cartilage or fat and this would appear to be the usual origin of these unusual mammary tumours which are described later.

Fibroblastic activity is found in a variety of lesions other than sarcoma. Certain benign fibroadenomas are peculiarly cellular and indeed may justify the concept of

border-line tumours. It is in these that the presence or absence of myxoid tissue is of special significance. Stout (1949) considered that "there is no accurate way to distinguish histologically between fibroma and fibrosarcoma" and Wilson (1945) suggested that "one has to be governed by whether or not the lesion grows to a large size and is persistent in growth". Mackenzie (1964) also considered the danger of a diagnosis of a benign condition when dealing with fibrosarcomas. Other lesions of unknown etiology of possibly inflammatory or traumatic origin are associated with proliferation of fibroblasts. The histological picture in such cases may be equivocal but the presence of inflammatory cells would indicate the correct diagnosis. There seems little justification for such terms as pseudosarcomatous fasciitis (Stout and Lattes, 1968).

In this study, the fibroblastic tumours are presented at greater length and illustrated more profusely than other types not only because of their greater frequency but also because they illustrate the essential underlying pathology of a whole group of malignant mesenchymal tumours. They demonstrate the development of a malignant neoplasm from a benign precursor as traced in the series described under Evolution (figs. 235 - 262). They indicate the changing architecture from the vascular myxoid tissue, scarcely in itself recognisable as neoplastic, to the characteristic fibrosarcoma. Furthermore, they illustrate the metamorphosis from the ordinary fibrosarcoma to osteosarcoma, chondrosarcoma and liposarcoma.

Fibrosarcoma.

| Series | Reference | Age | Duration of Tumour (years). | Type | Nodes | Therapy | Outcome in years. | Metastases |
|--------|-----------|-----|-----------------------------------|------------------------------------|-------|------------------------------------------|--------------------------------------------------------|---------------------------------------------------|
| 1. | 1291 | 74 | 1+ | Fibrosarcoma | - | Simple mastectomy | Alive 1 ⁷ /12 | - |
| 2. | 1283 | 64 | 1/12 | do. | - | Simple mastectomy | Alive 2 ¹ /12 | - |
| 3. | S.6. | 63 | 6/12 | do. | - | Local excision | Died 8 ¹¹ /12 (Carc. in other breast) | - |
| 4. | S.96 | ? | - | do. | - | Simple mastectomy | ? | - |
| 5. | S.23 | 70 | - | do. | - | Simple mastectomy | ? | - |
| 6. | S.171 | 60 | 6/52 | do. | - | Blopsy | Died 6/12 | - |
| 7. | 1198 | 26 | 11. | do. | - | Local excision | Recurrence & death. | Scalp and groin. |
| 8. | 1278 | 48 | 2.5/52 | do. | - | Simple mastectomy + irradiation. | Alive 3 ⁶ /12 | - |
| 9. | 1317 | 42 | ? | do. | - | Simple mastectomy | Alive 1 ¹ /12 | - |
| 10. | S.49 | - | ? | Fibrosarcoma with fibroadenoma | - | Radical mastectomy | - | - |
| 11. | S.16 | 69 | 3/12 | Fibrosarcoma | - | Radical mastectomy | Alive 8 ⁷ /12 | - |
| 12. | S.73 | 42 | 4/12 | do. | - | Irradiation and mastectomy | Died | Skin Lungs Liver Adrenal S.intestine. |
| 13. | S.10 | ? | ? | do. | - | Simple mastectomy | ? | - |
| 14. | 1262 | 72 | 3/12 | Fibrosarcoma + small carcinoma. | - | Simple mastectomy | Alive 1 ¹ /12 | - |
| 15. | S.110 | 45 | 6 Rapid 2/12 | Fibrosarcoma | - | Simple and later Radical mastectomy. | 2 Recurrences Died 5 ¹⁰ /12. | - |
| 16. | B.25 | ? | ? | Fibrosarcoma | - | Simple mastectomy | ? | - |
| 17. | S.24 | 59 | ? | Fibrosarcoma | - | Radical mastectomy | ? | - |
| 18. | S.91 | 43 | ? | do | - | Local excision | ? | - |
| 19. | S.90 | 62 | ? | do. | - | Radical mastectomy | ? | - |
| 20. | S.52 | 37 | 3/52 | do. | - | Local excision and radical mastectomy | Alive 4 ⁹ /12 | - |
| 21. | S.116 | 71 | 8/12 | do. | - | ? | ? | - |
| 22. | S.139 | 78 | 6/12 | do. | - | Simple mastectomy | ? | - |
| 23. | S.177 | 64 | Several/12 | do. | - | Radical mastectomy | Alive 6 ⁷ /12 | - |
| 24. | S.29 | 53 | 6. | do. | - | ? | ? | - |
| 25. | S.22 | ? | ? | do. | - | ? | ? | - |
| 26. | S.169 | 69 | 40 | do. | - | Simple mastectomy | ? | - |
| 27. | S.111 | 38 | 1. | do. | - | Simple mastectomy | - | - |
| 28. | S.158 | 32 | No delay | do. | - | Radical mastectomy | Alive 8/12 | - |
| 29. | S.139 | 78 | 6/12 | do. | - | Simple mastectomy | ? | - |
| 30. | S.108 | 66 | 1/12 | do. | - | Simple mastectomy & irradiation. | Alive 5. | - |
| 31. | S.175 | 60 | Few/12 | Fibrosarcoma | - | Local excision | ? | - |
| 32. | S.116 | 71 | 8/12 | Fibrosarcoma | - | Simple mastectomy | ? | - |
| 33. | S.140 | 75 | ? | do. | - | ? | Died 1. | Lungs. |

Case 1.

1291.

History: The patient, aged 74 years, had known of a tumour in one breast for more than a year but operation was refused. She was finally admitted to hospital as an emergency with considerable haemorrhage from this breast which had ulcerated.

Examination: The whole breast was replaced by a large ovoid tumour, sharply defined, lying below the nipple (fig. 1.) and showing areas of atrophic and ulcerated skin. It was removed by simple mastectomy. The tumour on transection showed dilated clefts and poorly separated lobular masses with opaque and translucent areas. Appearances were those of a giant fibroadenoma which might be undergoing sarcomatous change.

Histology: The basic fibroadenomatous structure is confirmed with an unusual formation of prominent defined cellular fibroblastic patches (figs. 2, 3 & 4), with some mitotic activity. Some areas show closely approximated stromal and epithelial proliferation (fig. 5). The translucent areas are of typical myxoid tissue with numerous capillaries (fig. 6). There is no pleomorphism but the mitotic activity and cellularity indicate an early fibrosarcomatous condition in all of the eight areas examined rather than a "border-line" tumour. This is a recent case and the patient remains well with no recurrence 1 year 7 months after operation.

Case 1.



Fig 1.

$\times \frac{1}{2}$.

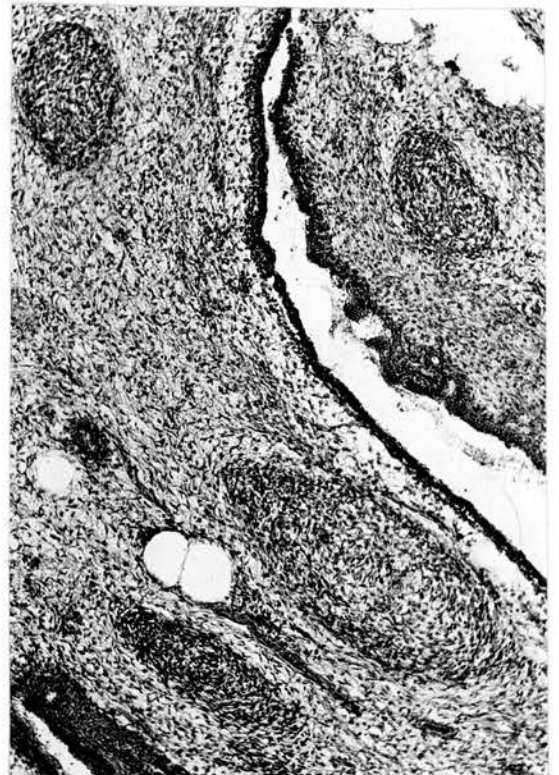


Fig. 2.

$\times 70$.



Fig. 3.

$\times 100$.

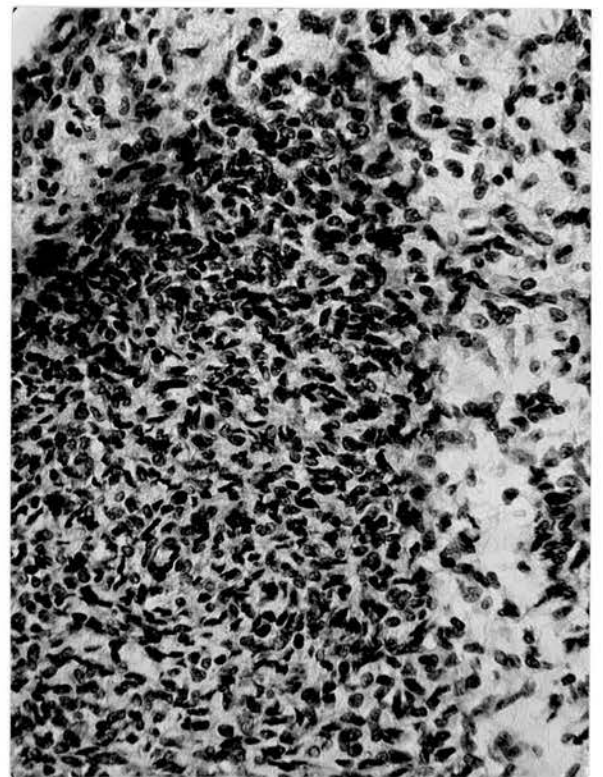


Fig. 4.

$\times 250$.

Case 1.

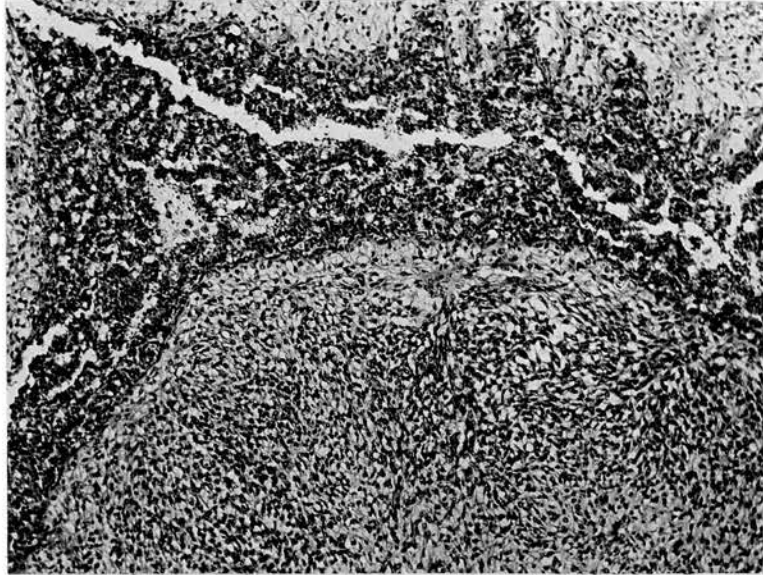


Fig. 5.

x75.

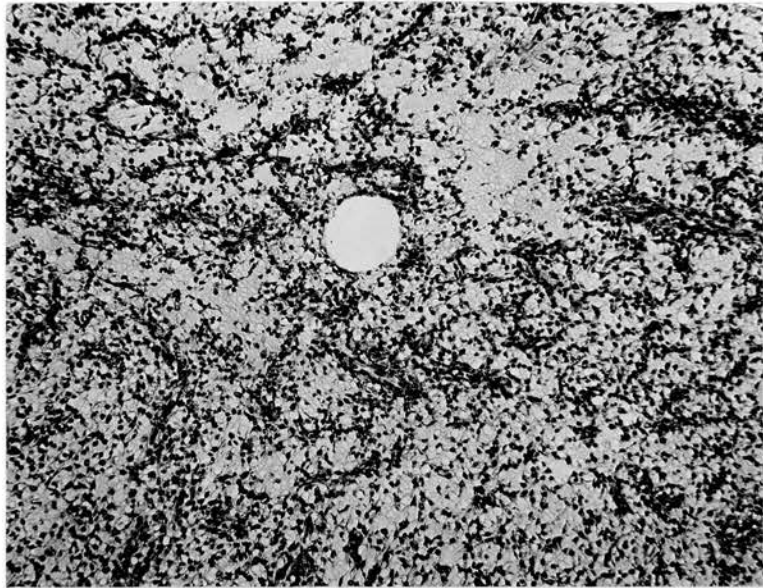


Fig. 6.

x90.

Case 2.

1283.

History: The patient aged 64 years, of heavy physical build with fat-laden breasts, noted a swelling in a breast for only 1 month. There was no pain or nipple discharge.

Examination: The breast is grossly enlarged and spherical with flattening of the nipple and some discoloured and slightly bosselated skin. On transection a large amount of dark fluid poured out. The tumour is well demarcated, almost replacing the breast tissue and the large lobulations have become separated, some of the spaces between them containing blood (fig. 7). Strands of fibrous tissue show a translucent white appearance, a picture pointing to sarcomatous change.

Histology shows a fibrosarcoma which has developed in a cystic giant fibroadenoma parts of which are still evident (fig. 8). There are large areas of purely stromal tissue of varying cellularity and mitotic activity (fig. 9), but little pleomorphism. The epithelium of the large cystic spaces shows no neoplastic proliferation. This is a recent case and the patient is alive and well 2 years 1 month after operation.

Case 2.

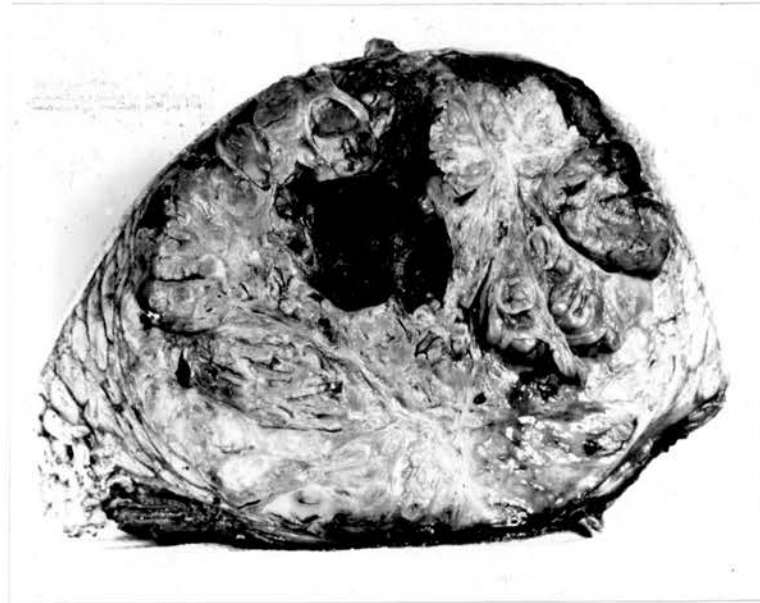


Fig. 7.

$\times \frac{1}{2}$.

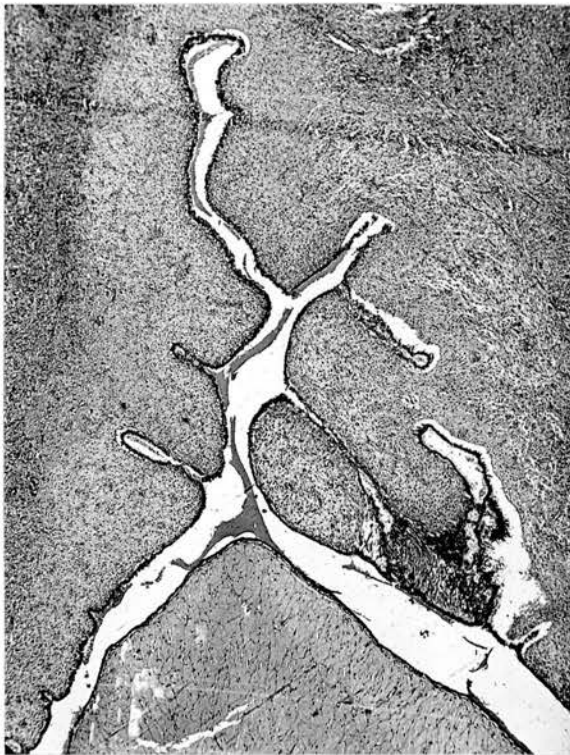


Fig. 8

$\times 30$.

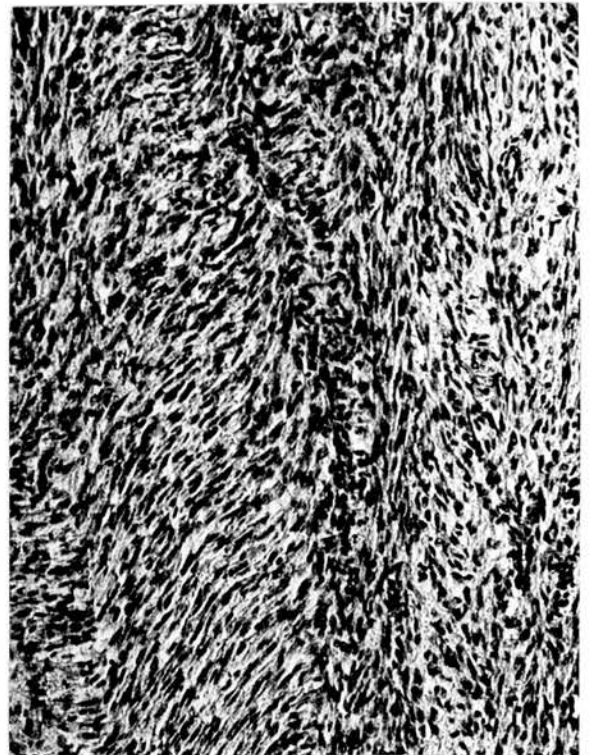


Fig. 9.

$\times 150$.

Case 3.

S.6.

History: The patient, aged 63 years, noticed a tumour in one breast for 6 months.

Examination showed a defined tumour which clinically suggested a fibroadenoma but was irradiated before simple mastectomy. A rough wash drawing, actual size, (fig. 10) and a section of the tumour (fig. 11) show the macroscopic appearance.

Histology: Defined polypoid masses now denuded of covering epithelium point to an intracanalicular fibroadenomatous histogenesis (figs. 12 & 13). The irradiated effect on some areas is shown in fig. 14 but much of the growth is an active and somewhat pleomorphic fibrosarcoma (fig. 15).

Four years later she had a primary carcinoma of the other breast removed with invaded axillary nodes. This second tumour proved fatal, death occurring 8 years 11 months after the excision of the sarcoma which had not recurred.

Case 4.

S.96.

History: An old case cut as a whole breast section with no clinical data available. About a quarter of the area is an intracanalicular fibroadenoma (right side). The malignant part is very cellular, vascular, fairly well defined and non-cystic (fig. 16).

Histology: Hyalinized and cellular polypoid masses are in close relation where the benign and malignant areas meet (fig. 17). The capillary vascular network, sharply defined against a myxoid stroma (fig. 18) is less distinct where there is more perivascular cellularity (fig. 19). It is almost obliterated in the pleomorphic more cellular areas of the tumour with scattered giant cells (fig. 20).

Case 3.

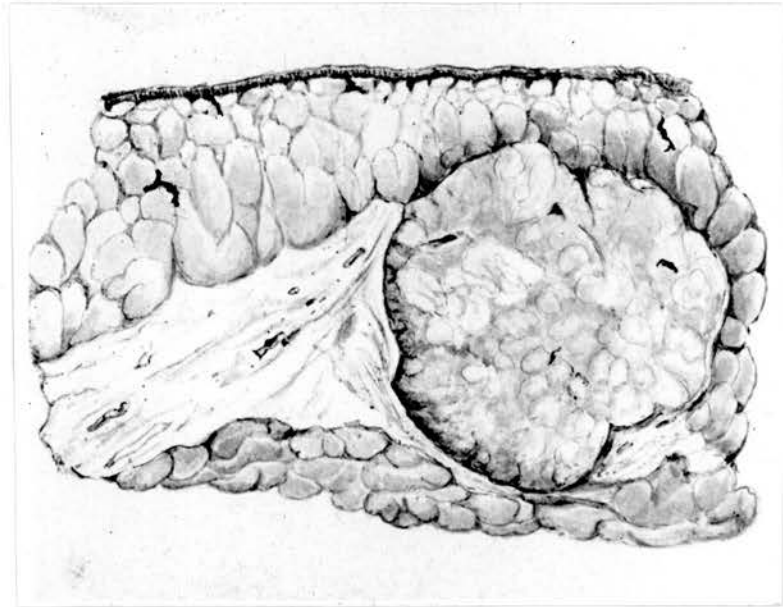


Fig. 10.

x 1.5.

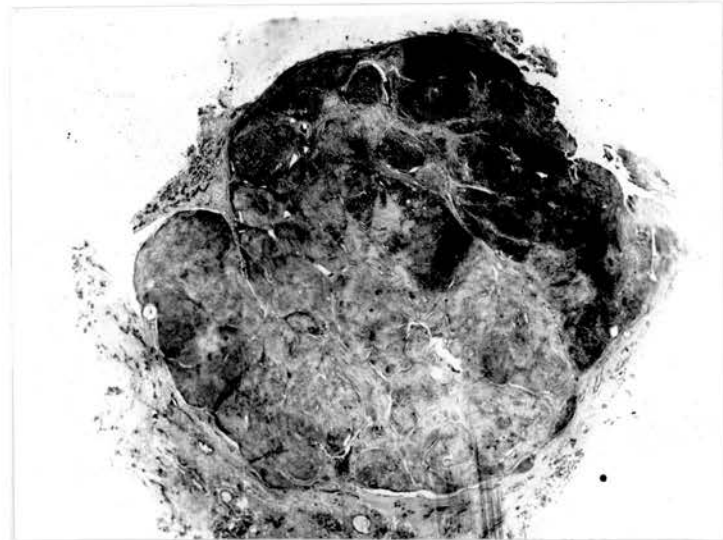


Fig. 11.

x 2.

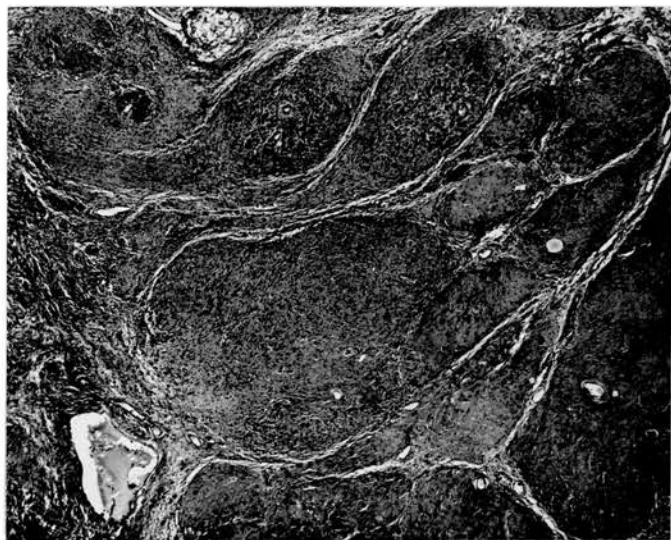


Fig. 12.

x 16.

Case 3.

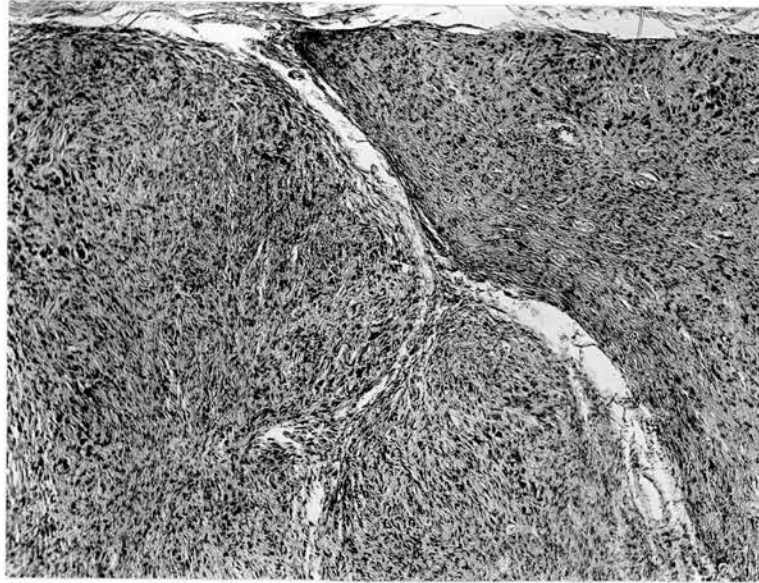


Fig. 13.

x50.

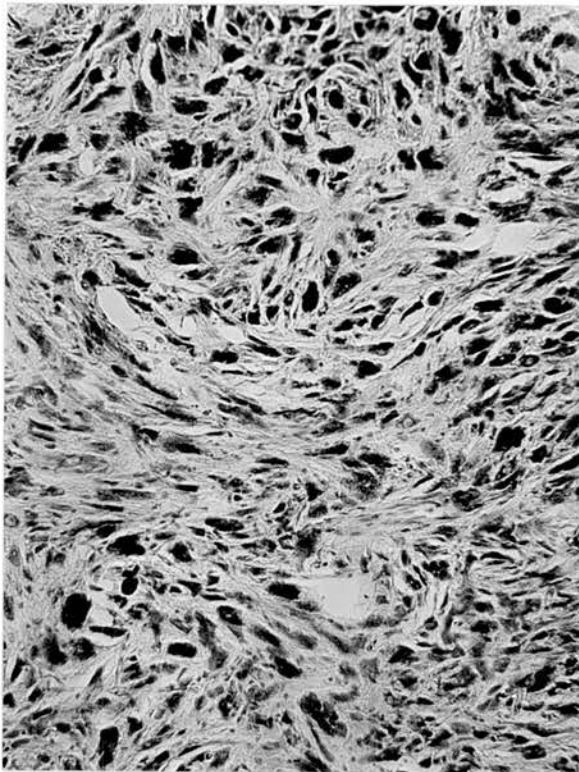


Fig. 14.

x120.

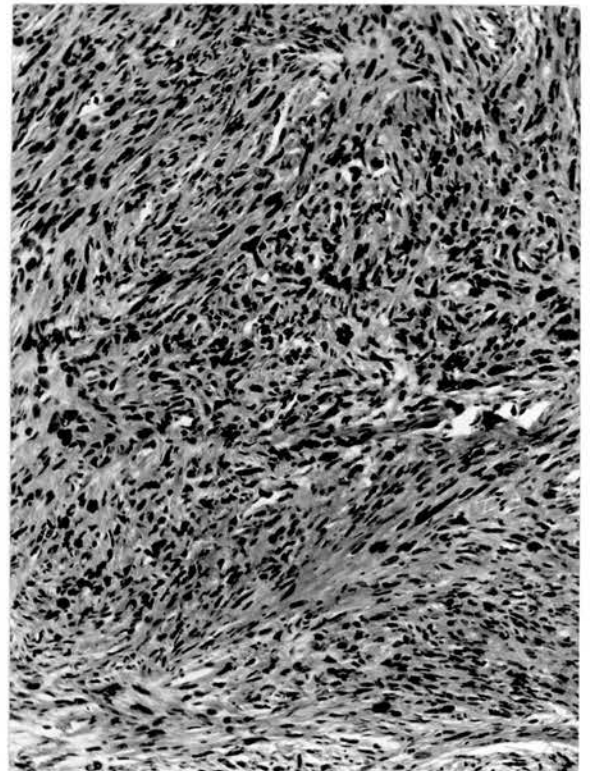


Fig. 15.

x85.

Case 4.

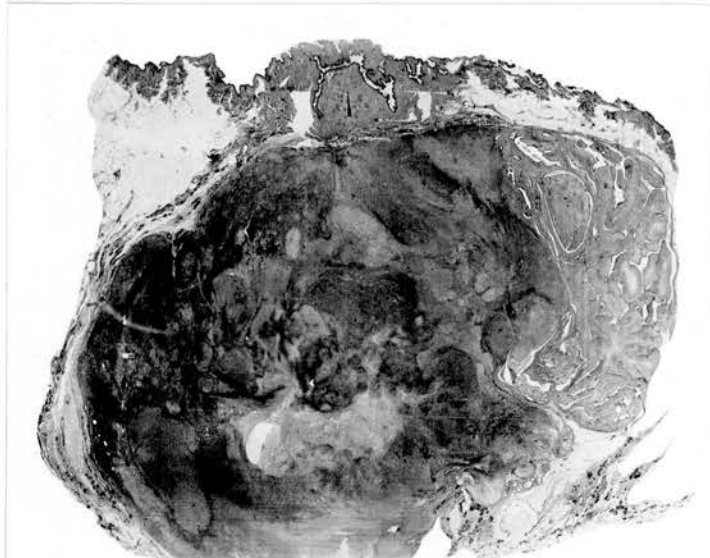


Fig. 16

x1.

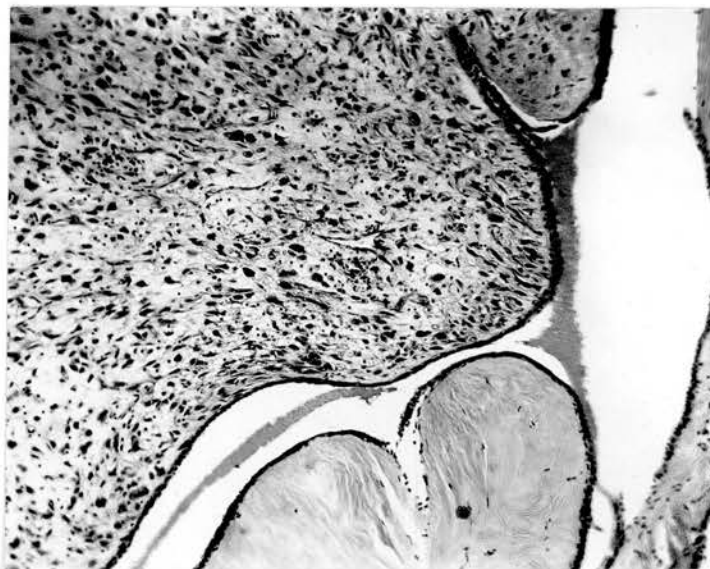


Fig. 17.

x 50.

Case 4.

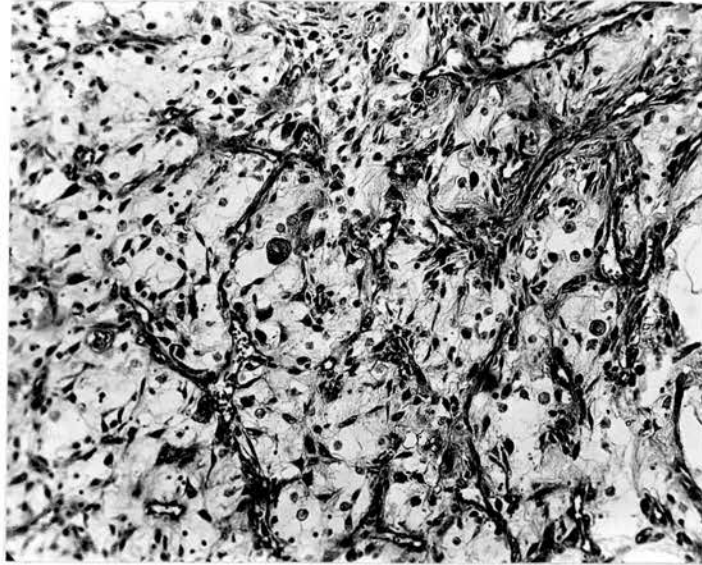


Fig. 18.

× 150.

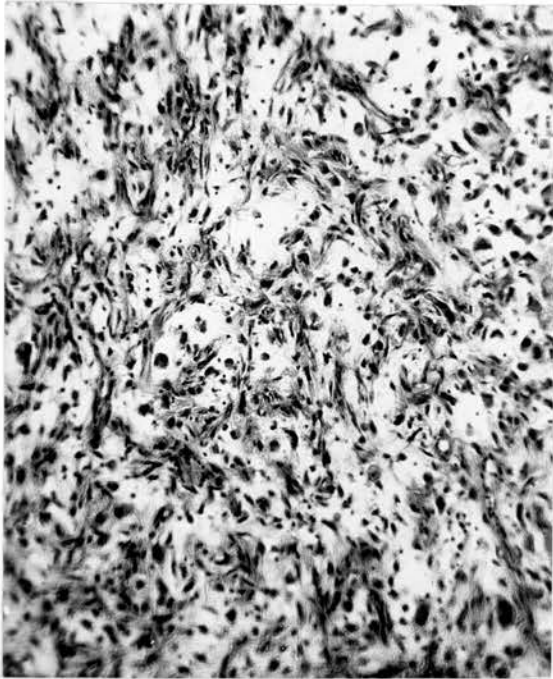


Fig. 19.

× 120.

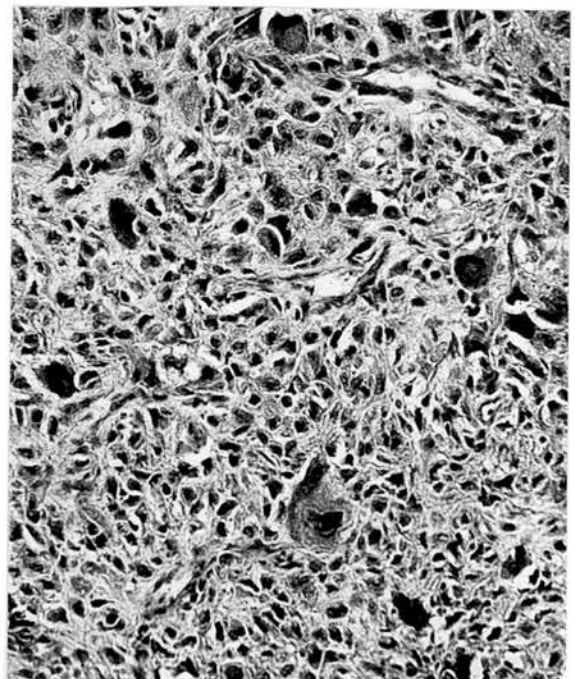


Fig. 20.

× 150.

Case 5.

S.23.

History: The patient aged 70 years was aware of a swelling in one breast for over 3 months. It had gradually become more prominent and tender with reddened skin over it. Her doctor diagnosed chronic mammary abscess and wanted to incise it but it was decided for her to see a surgeon.

Examination showed a large swelling on the outer half of the breast covered by purplish skin (fig. 21). There was definite fluctuation but no axillary nodes were palpable. The swelling was incised and showed grumous fluid and masses of obvious tumour suggestive of an intracystic malignant papilloma. Radical operation followed. There was no invasion of muscle. A few soft enlarged axillary nodes were removed for examination.

Histology: The tumour is a rapidly growing sarcoma. There is in general, marked capillary vascularity (fig. 22). The cells show great variation in size with mitotic activity (fig. 23). In some areas, blood vessel walls are formed by multi-layered malignant cells with numerous mitotic figures (fig. 24). An unexpected finding is a malignant duct in the middle of the tumour (fig. 25).

Case 5.

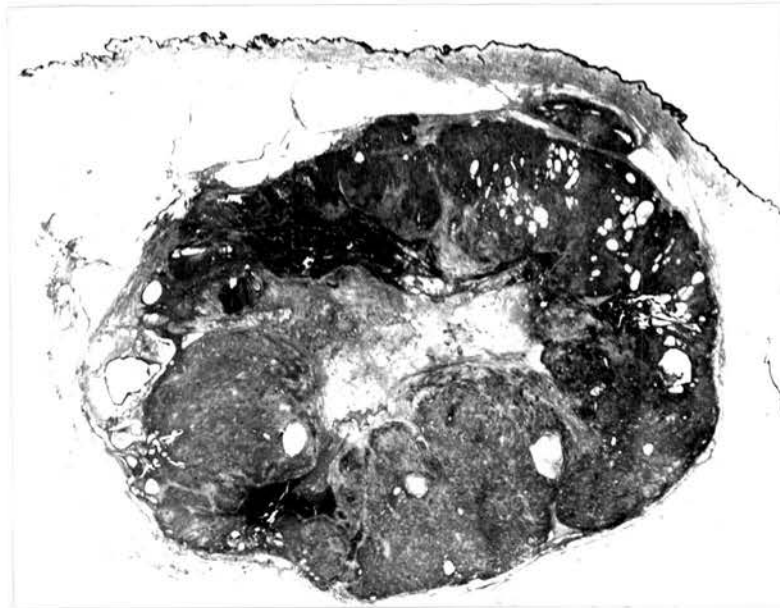


Fig 21.

x1.

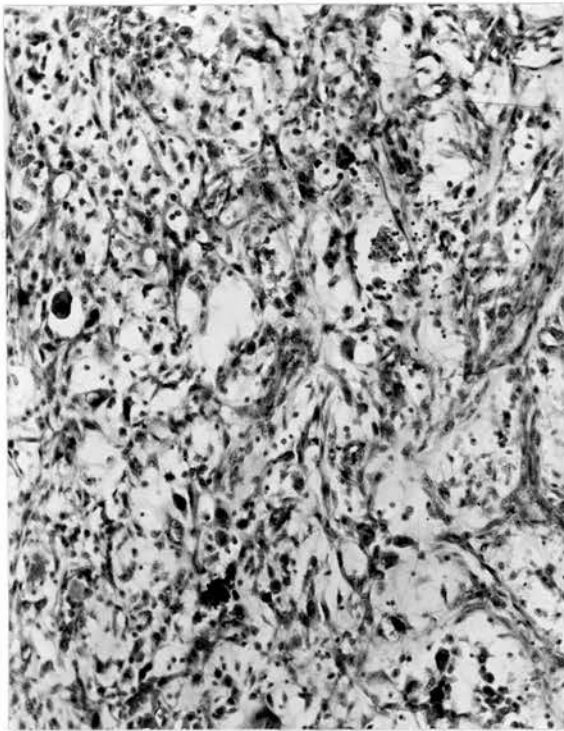


Fig. 22.

x90.

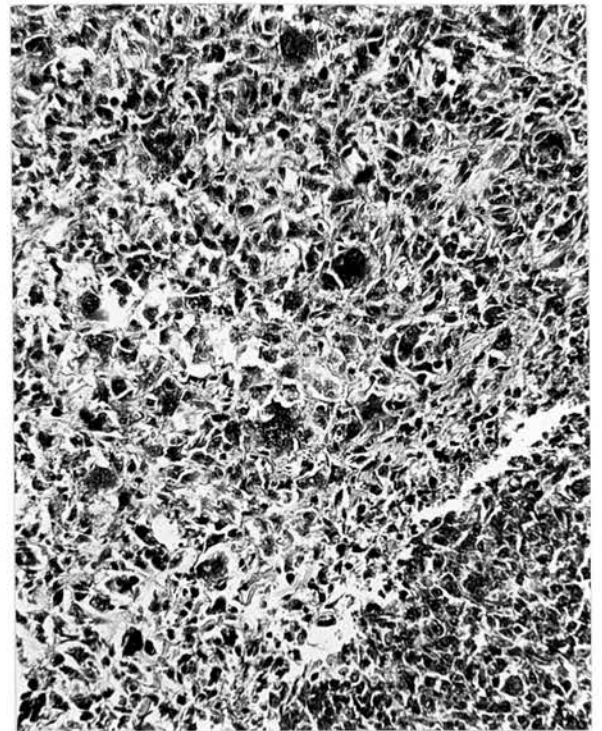


Fig. 23.

x100.

Case 5.

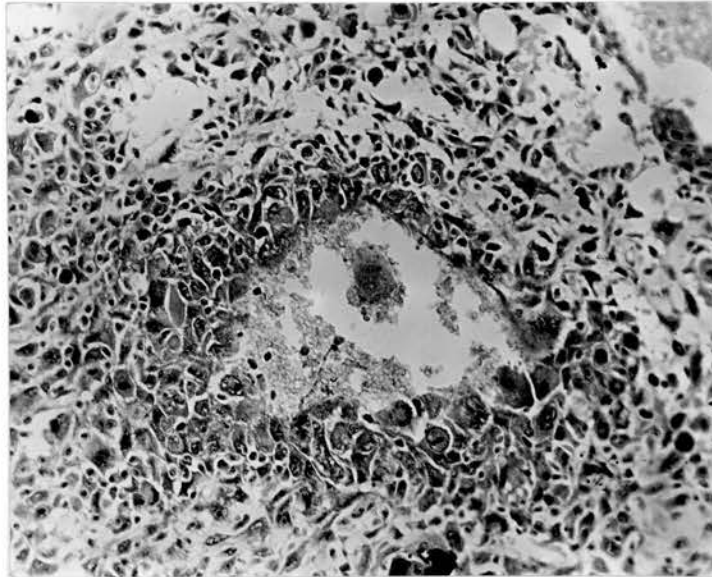


Fig. 24.

x 200



Fig. 25.

x 40.

Case 6.

S.171.

History: The patient aged 60 years gave a history of a lump in the right breast for 6 weeks.

Examination: There was no loss of weight but the breast was fixed to skin and deep muscle with superficial nodular masses and discoloration of the skin (fig. 26). No nodes were palpable. She was treated with Testosterone for 6 weeks before a biopsy was taken. Radiographs of the chest 3 days before biopsy showed a homogeneous opacity in the lower and mid zones and also a deposit in the base of the upper lobe. No further operation was attempted and irradiation had no effect. Three months later the tumour was growing rapidly with progressive fungation and loss of over a stone in weight. She died at home 6 weeks later ^{with lung metastases} a total survival of 6 months after the first examination. There was no autopsy. It is instructive that this was the only mammary sarcoma the pathologist had seen in 10 years.

Histology: The biopsy tissue shows an area near the skin with capillary proliferation in a cellular fibromyxoid tissue (fig. 27). There are numerous mitotic figures (fig. 28) and much necrosis in some areas. Deeper in the tumour, there is a more pleomorphic picture (fig. 29).

This was a very advanced tumour with metastasis when first seen and palliative measures had little if any effect.

Case 6.



Fig. 26.



Fig. 27.

x50

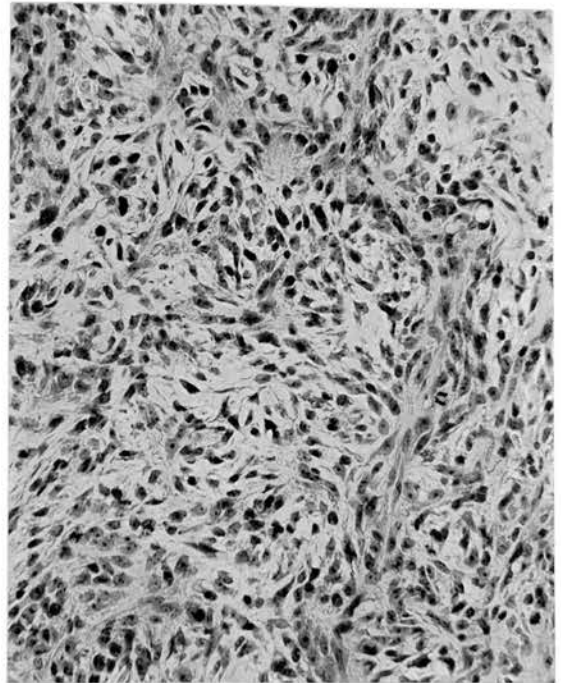


Fig. 28.

x250.

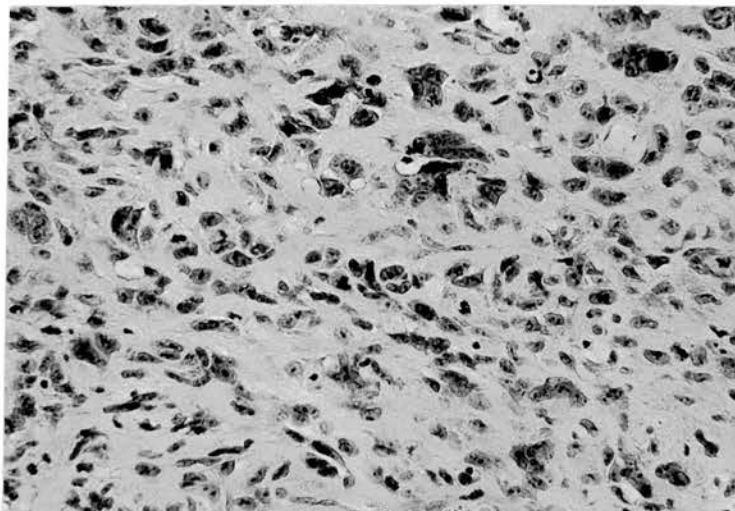


Fig. 29.

x250.

Case 7.

1198.

History: The patient noticed a lump in one breast when about 15 years old. She concluded that it was cancer and, convinced it would soon prove fatal, she evaded examination and later refused marriage. When changing employment, she had to have a routine medical examination and the tumour was revealed. It suggested a fibroadenoma and she agreed to its removal.

Examination showed "an encapsulated mass 13 x 12 x 5 cm. containing haemorrhagic cysts in fatty material". It suggested lipoma and was excised locally.

Histology: This tissue was reported elsewhere as a mixed mesenchymal tumour of unusual type, mainly myxolipomatous but with cellular areas of spindle-cell tissue with hyperchromatic, irregular nuclei. Intimate relation to abnormal blood vessels suggested leiomyoma but further treatment was not considered necessary and the patient, on being informed the growth was not malignant, got married. Two months later she found a small nodule near the operation scar on the shoulder which grew very rapidly (fig. 38) and was only temporarily controlled by irradiation. Later, more recurrences appeared in the scalp above the left orbit and in the right groin. The latter grew to the size of a small tangerine orange in a week. Her condition deteriorated rapidly and she died aged 27, 12 years after her initial discovery of tumour at 15 years. No autopsy was requested. Tissue from the primary mammary growth and the recurrent tumour on the shoulder was sent me for examination.

The primary tumour shows great variation of structure. Remnants of a benign fibroadenomatous structure are still present in a myxoid fatty vascular background (fig. 30). Much of the growth is myxosarcomatous in type with adjacent fibrosarcoma (fig. 31). The periphery shows a more cellular fibrosarcoma in juxtaposition to a myxolipomatous tissue (fig. 32) and small detached nodules are forming in this fatty background (fig. 33) with later diffuse infiltration and dilated blood vessels (fig. 34). Some peripheral areas show a stranded picture of cellular fibrosarcoma, less cellular lipofibrosarcoma and almost pure lipomatous tissue (fig. 35). This lipomatous picture is seen in figs. 36 & 37 at low and higher magnification and suggests an early liposarcomatous change. The amount of

fatty tissue associated with the tumour explains the appearance at the first operation. The recurrence in the scar on the shoulder (fig. 38) shows a purely fibrosarcomatous structure, with much infiltration by inflammatory cells (fig. 39) and the spread into muscle on its deeper aspect (fig. 40).

This is an instructive case indicating the time taken for malignant change to develop in a fibroadenoma of a young subject. The variation of its structure and its difficult interpretation with the abundant lipomatous component justify its very ample illustration.

Case 8.

1278.

History: The patient is now aged 43 years. While nursing her only child 8 years previously, a lump was found in one breast which resolved by fomentations. She is now menopausal and complains of heaviness and hardening of this breast noticed for 2½ weeks.

Examination: The tumour was diagnosed provisionally as carcinoma because hard and irregular in outline, though mobile. There was no discharge, no nipple retraction and no palpable axillary nodes. X-ray examination was negative for metastasis in lungs or bones. At operation, the tumour suggested a fibroblastic growth with some cyst formation. It was treated by simple mastectomy and irradiation.

Histology: An intracanalicular fibroadenomatous structure with ducts distorted by polypoid stromal growth showing great variation in cellularity (fig. 41). Reticulin stain emphasizes the thick capsule and the abundant fibroblastic tissue below (fig. 42). Some areas show numerous giant cells of osteoclast type in a very cellular matrix (fig. 43); in other areas a more malignant fibrosarcomatous picture is found, with spindle-cell tissue interspersed with single- and multiple-nucleated malignant giant cells (fig. 44). Mitotic figures are easily found in areas like figs 43 & 44. The patient was alive and well 3 years 6 months after operation.

This is a good example of a fibrosarcoma arising in an intracanalicular fibroadenoma.

Case 7.



Fig. 30.

x30

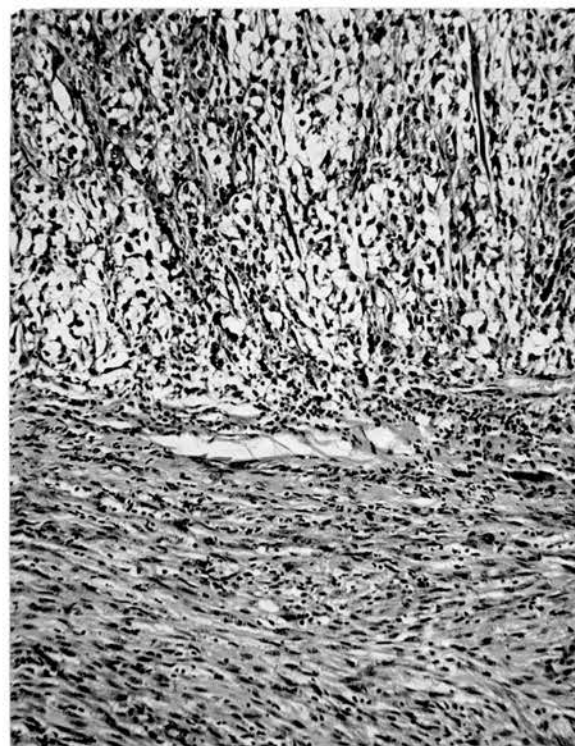


Fig. 31.

x100.

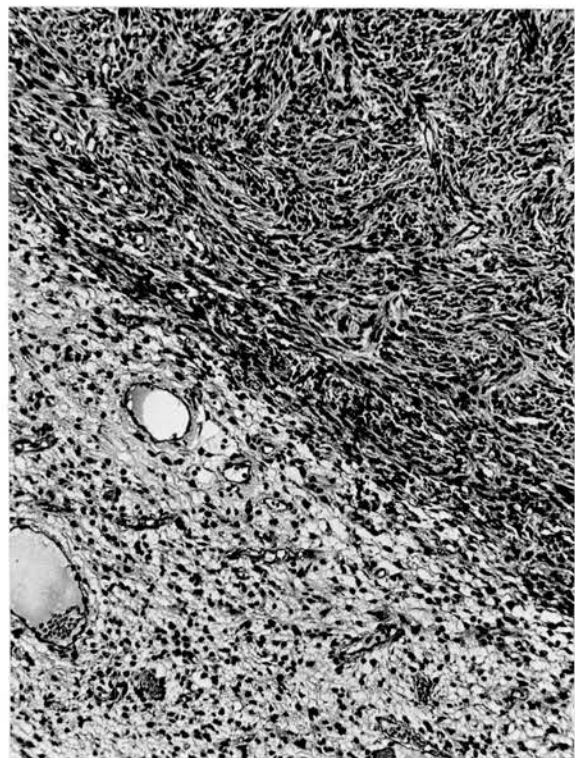


Fig. 32

x100.

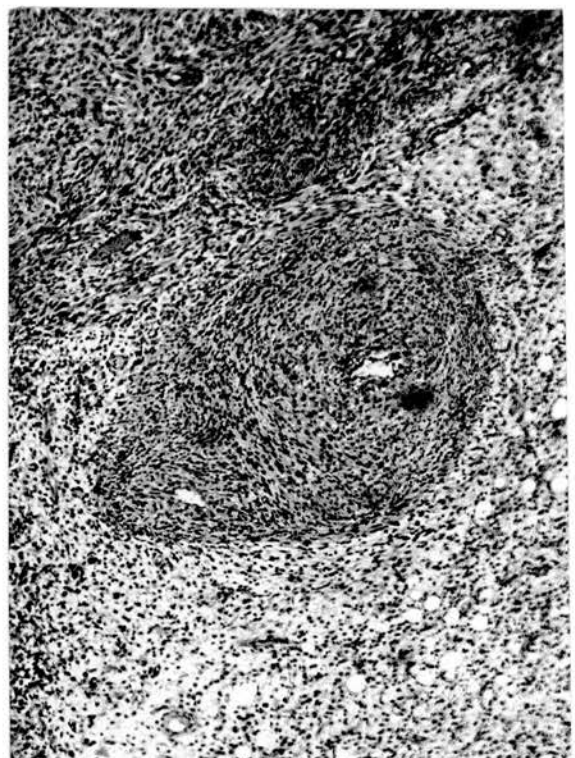


Fig. 33.

x 80.

Case 7.

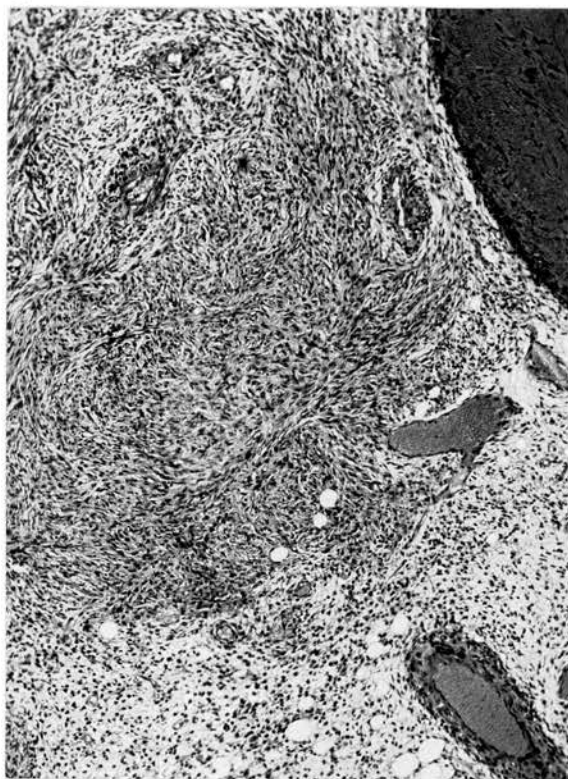


Fig. 34.

x65.



Fig. 35.

x100

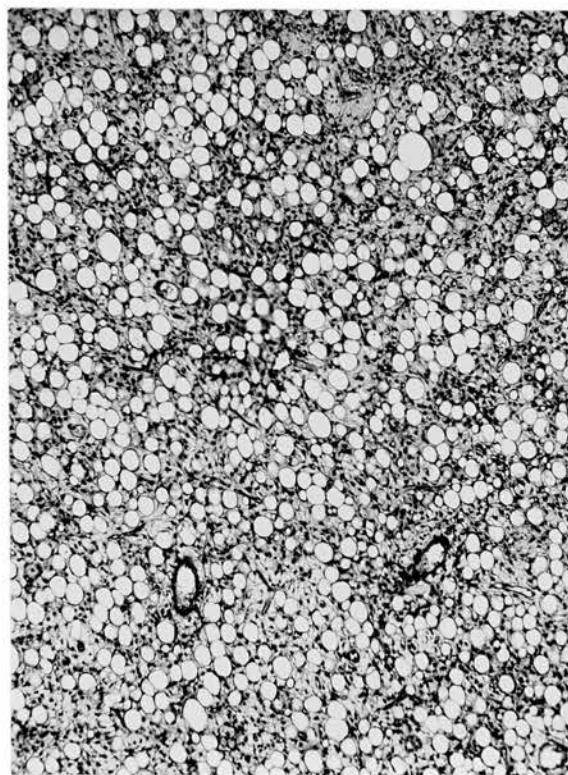


Fig. 36.

x65.

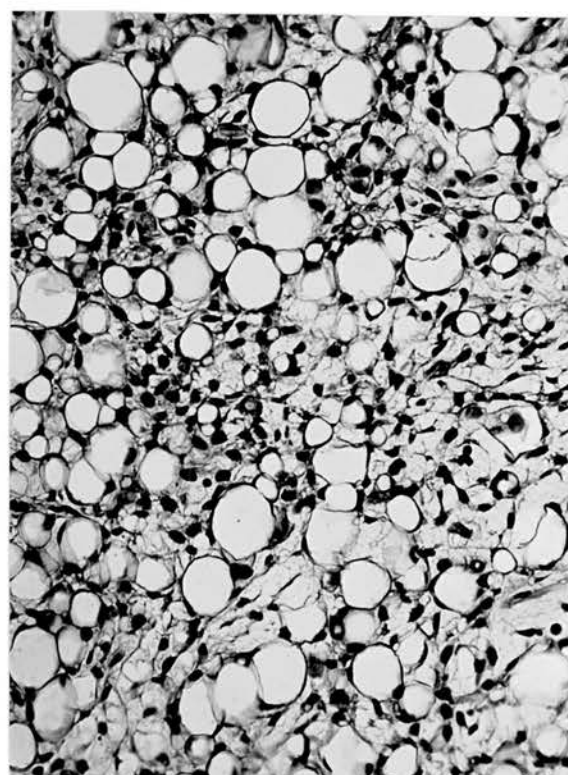


Fig. 37.

x250.

Case 7.



Fig. 38.

x1.

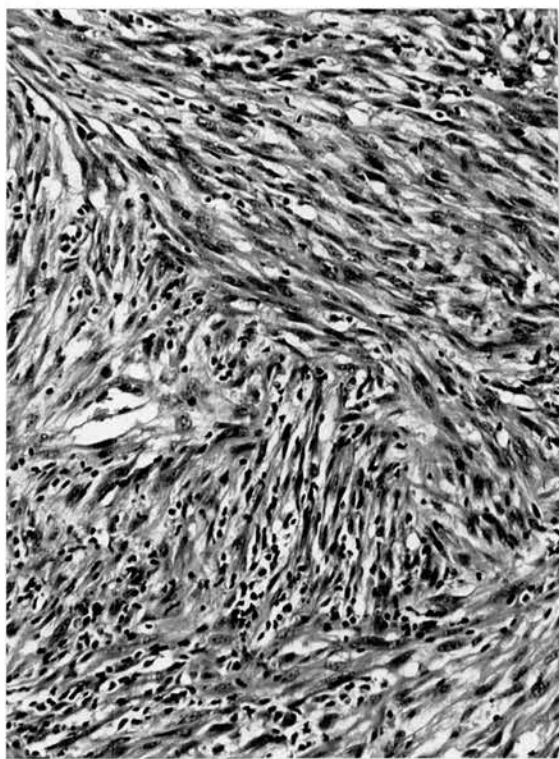


Fig. 39.

x150.

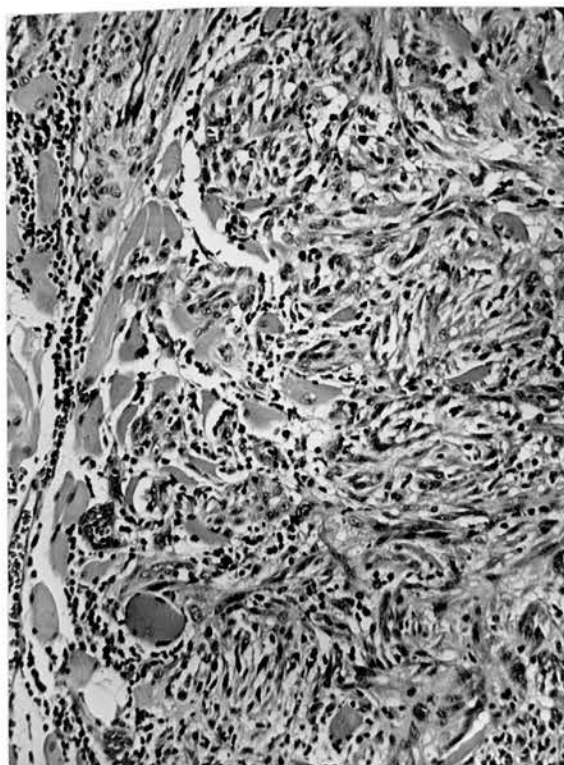


Fig. 40.

x150.

Case 8.



Fig. 41.

x30

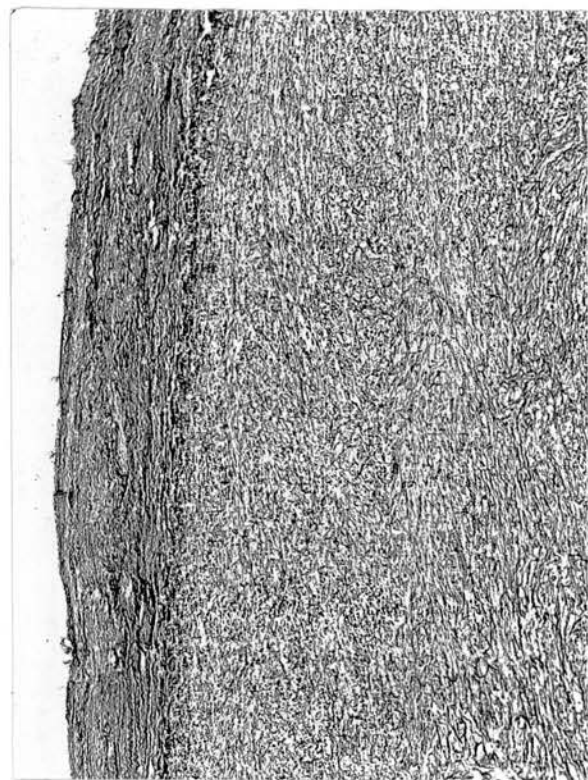


Fig. 42.

x 80.

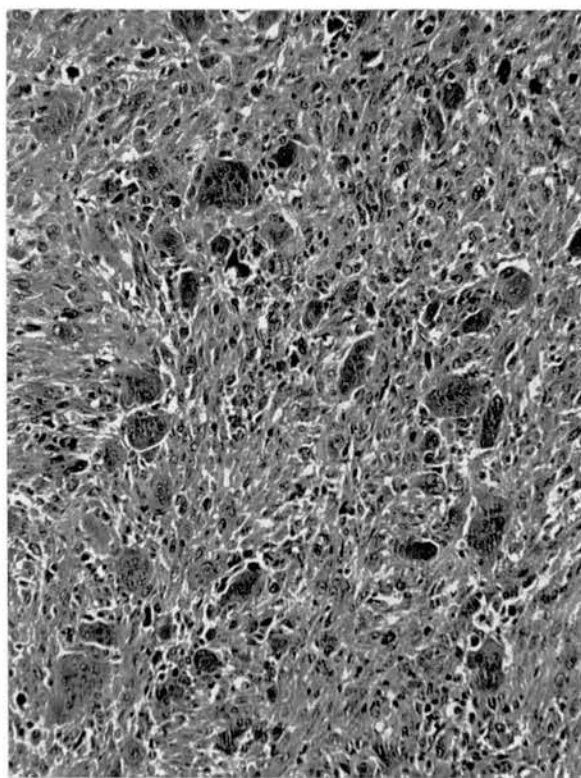


Fig. 43.

x120

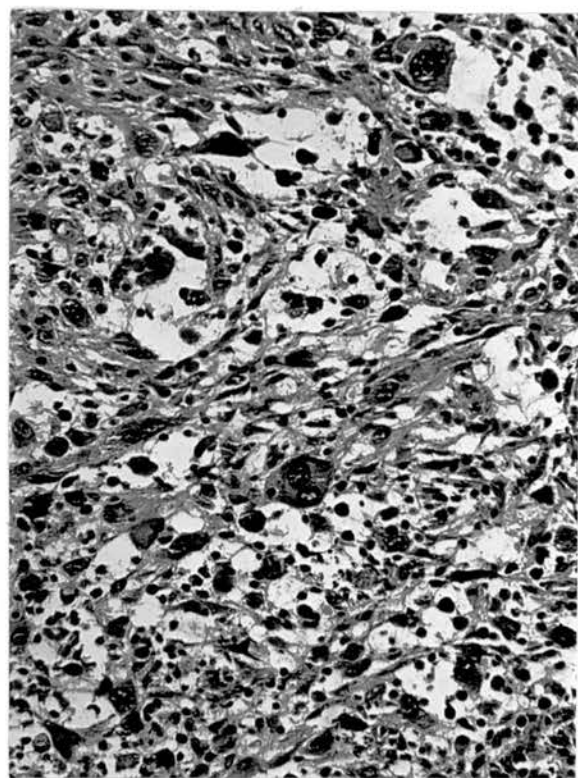


Fig. 44.

x150.

Case 9.

1317.

History: The patient was aged 42 years. A tumour in one breast became palpably larger in the 3 weeks between first inspection and admission to hospital.

Examination: At operation a firm, partly cystic tumour was found, greyish and fully 4 cm. in diameter. Transection showed some mucoid areas.

Histology: Five areas were sectioned, one of which shows an intracanalicular fibroadenomatous structure (fig. 45). The general appearance is of a well differentiated fibrosarcoma, in which mitotic figures are easily found (figs. 46, 47 & 48), with some mucoid areas. This is a recent case and the patient is alive and well 1 year 1 month after operation.

Case 10.

S.49.

History: An old case for which few data are available except removal of the breast by radical mastectomy.

Histology: A fibroadenoma mainly quiescent but with some cellular areas, lies in close juxtaposition to a sarcoma (fig. 49). The sarcoma, which contains a few scattered ducts, is highly vascular and of myxosarcoma type. There are numerous large, pleomorphic cells and abundant mitotic figures especially near capillaries (fig. 50). Some areas suggest an early chondroid metaplasia (fig. 51) but no material was available to confirm this by differential staining. Much of the malignant growth has become a solidly cellular fibrosarcoma. The axillary nodes were not invaded.

Case 9.



Fig. 45.

x35.

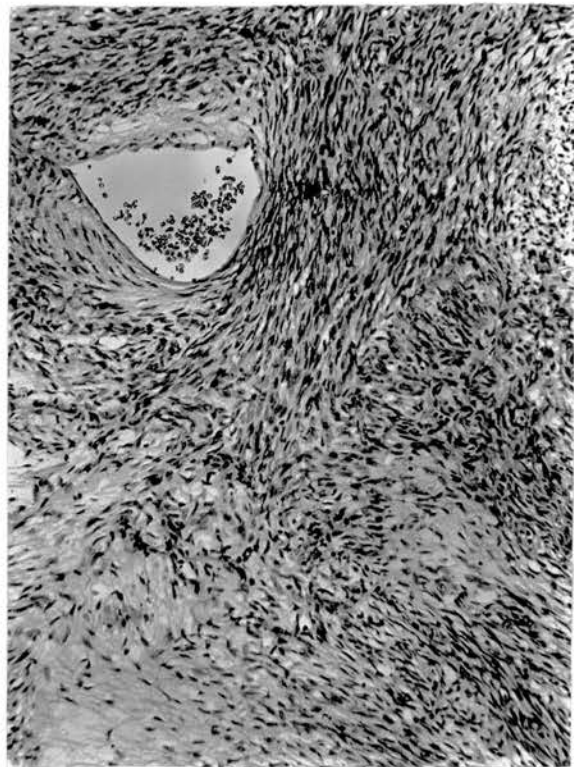


Fig. 46.

x100

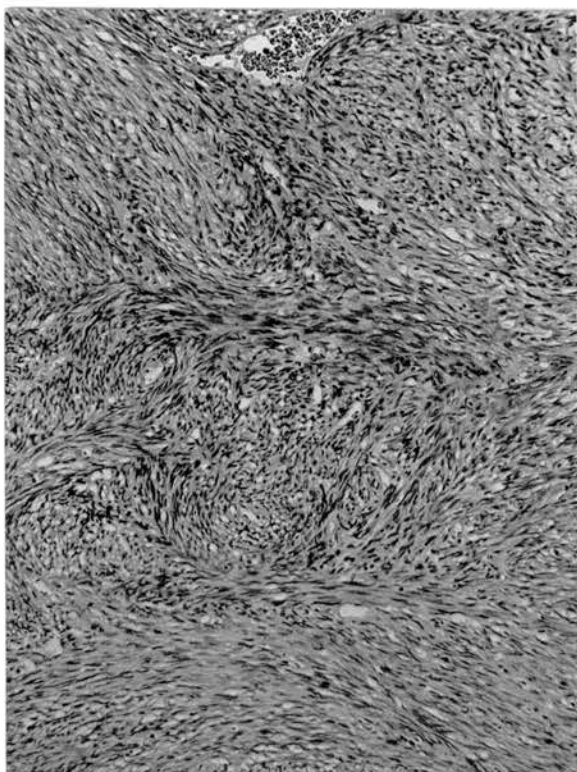


Fig. 47.

x100

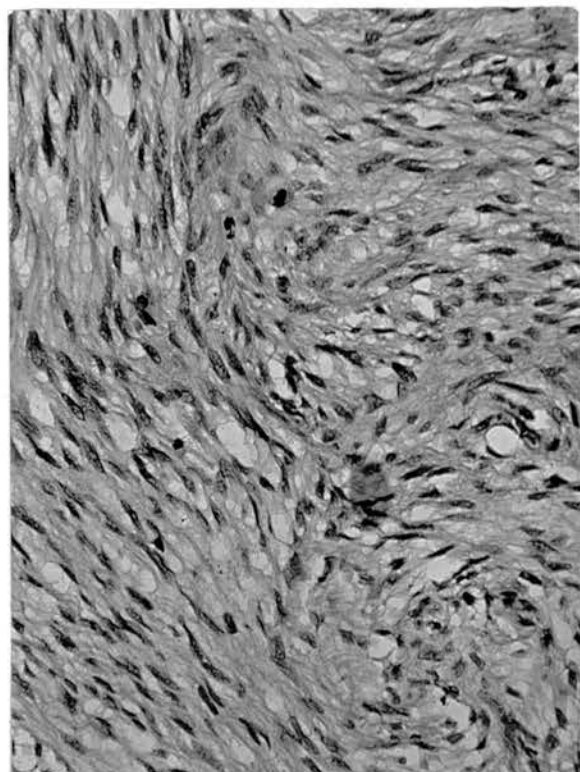


Fig. 48.

x300.

Case 10.

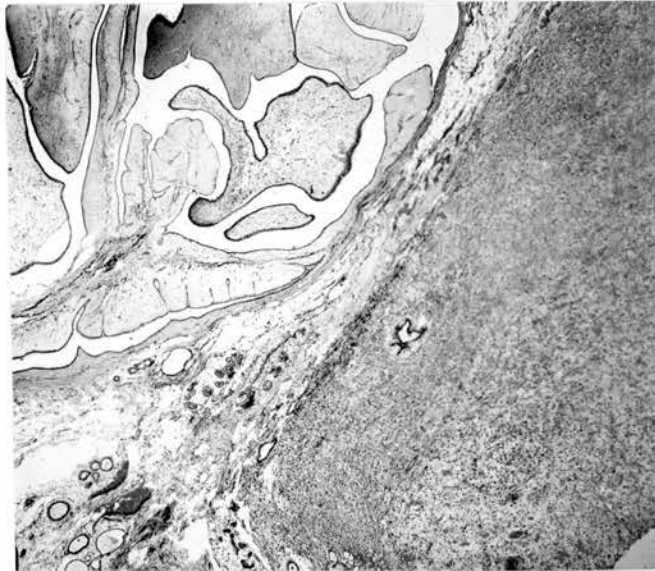


Fig. 49.

x 20.

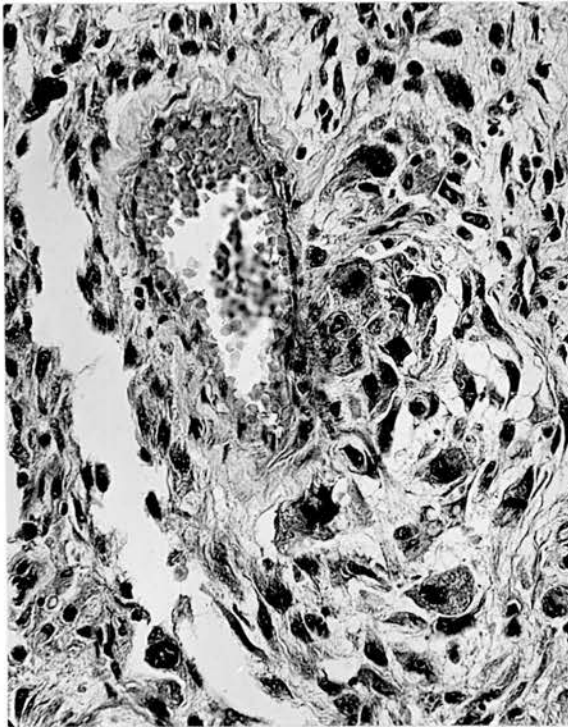


Fig. 50.

x 275

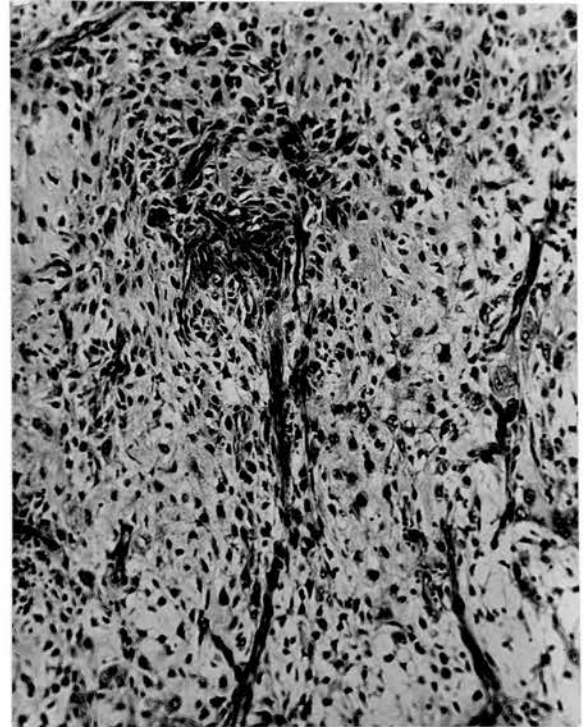


Fig. 51.

x 120.

Case 11.

S.16.

History: A private patient aged 69 years noticed a lump in one breast for 3 months.

Examination: No clinical data sent except "nature of tumour uncertain".

Radical mastectomy had been done.

Histology: The small piece of tumour sent showed a highly cellular fibrosarcoma with numerous mitotic figures in all 3 areas illustrated. An unaffected duct was found in the tumour (fig. 52) but no other evidence of possible fibroadenomatous histogenesis (fig. 53). The periphery was defined but without a capsule (fig. 54). The axillary nodes were largely fatty and showed no invasion. The patient was alive without recurrence 8 years 7 months later, a long survival for an apparently active advanced growth.

Case 12.

S.73.

History: The patient aged 42 years had noticed a very tender large swelling of the breast for 4 months.

Examination showed a solid tense swelling of the whole left breast with surrounding vascularity and fixation. There was a mass in the ipsilateral axilla. X-rays showed no chest deposits so irradiation was followed by mastectomy. She died 1 month later, 4 months after the first examination. At autopsy, metastases were found in the skin, lungs, liver, both adrenals and small intestine.

Histology: The primary area showed an ill-defined periphery where it was invading fat. Much of the tissue showed post-irradiation hyalinization (fig. 55), considered elsewhere as early osteoid change. No mammary glands were found. Some of the skin metastases show an active spindle-cell fibrosarcoma (fig. 56), others, a more pleomorphic structure (fig. 57). The lungs and adrenal deposits are also pleomorphic (figs. 58 & 59). No axillary tissue was sent.

This is the only case in the sarcoma series in which autopsy tissues were available

for examination. It is regretted that the axillary tumour was not sent as lymph node involvement in breast sarcoma is very unusual. Tumour could have spread from one of the nearby skin deposits or be tertiary and blood-borne to the axilla from the lung.

Case 13.

S.10.

History: An old case with few notes. The tumour was clinically malignant and radical mastectomy was done.

Examination: A defined, lobulated tumour. Transection showed two closely adjacent solid tumours (fig. 60) with little evidence of fibroadenomatous structure. Some soft, necrotic areas were recognised.

Histology: A fibrosarcoma with a few scattered remaining ducts. The structure was mainly spindle-celled with many mitotic figures (fig. 61) and much necrosis in the zones of perivascular cell survival (fig. 63). The tumour had ruptured the thin fibrous capsule with invasion of the pectoral fat. (fig. 62).

Case 14.

1262.

History: The patient aged 72 years had noticed a lump in one breast for 3 months. No other data available.

Histology: An intracanalicular fibroadenomatous structure with polypoidal masses covered by quiescent or multilayered epithelium (fig. 64). Other areas show a predominantly stromal proliferation with moderate mitotic activity (fig. 65). An unexpected finding unconnected with the fibroadenoma was a small epithelial growth apparently malignant and infiltrative (fig. 66) and originating in small ducts entirely filled with active cells. No data were given regarding lymph nodes. The patient was alive and well 13 months later. This is a rather doubtful early fibrosarcoma.

Case II.

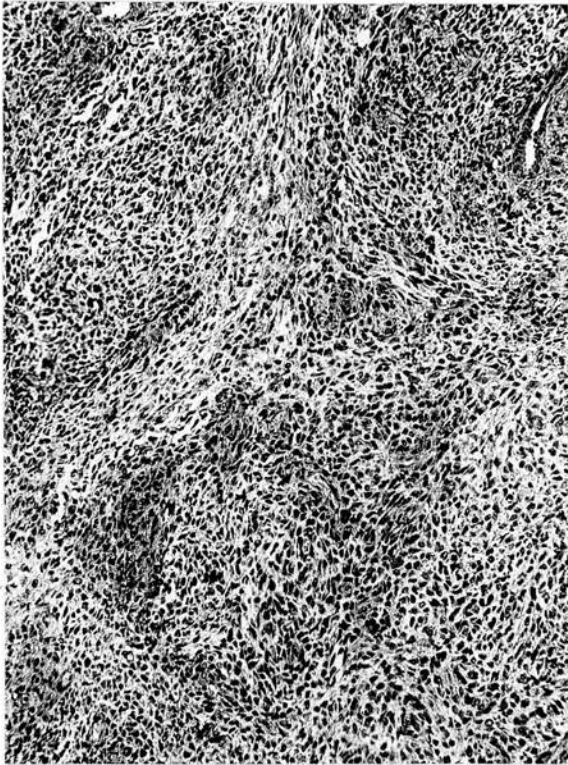


Fig. 52.

× 100

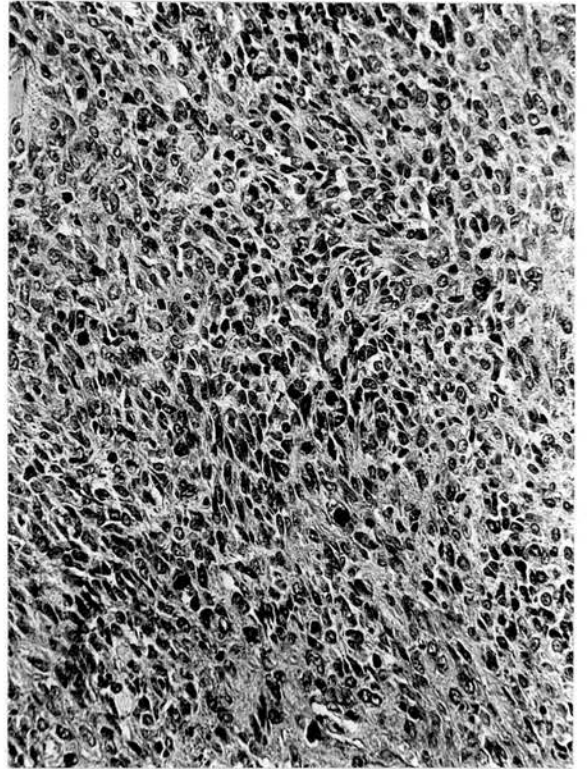


Fig. 53

× 225.

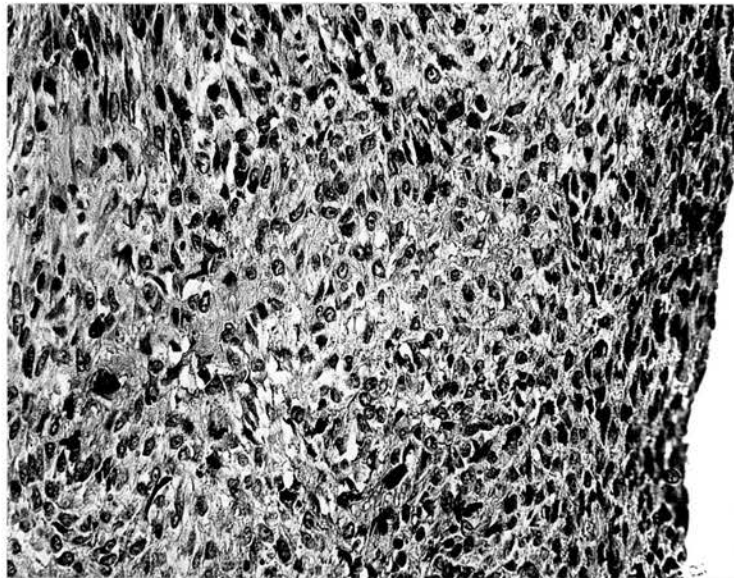


Fig. 54.

× 225.

Case 12.

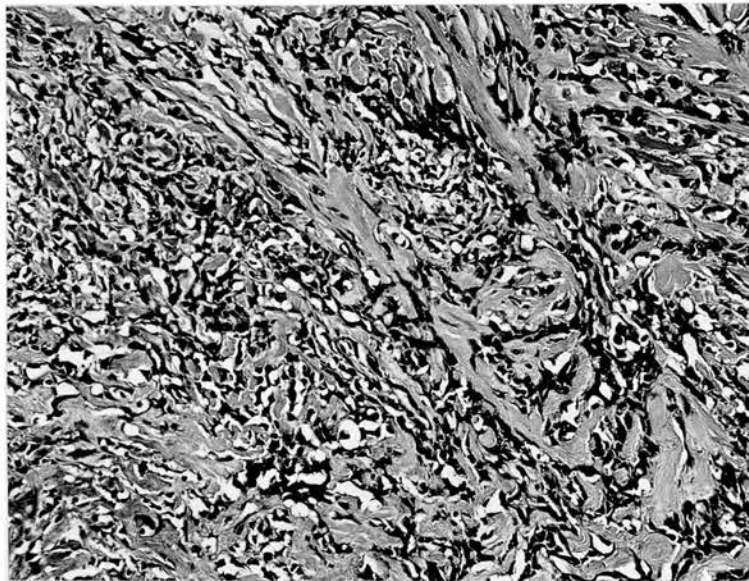


Fig. 55

x 100.

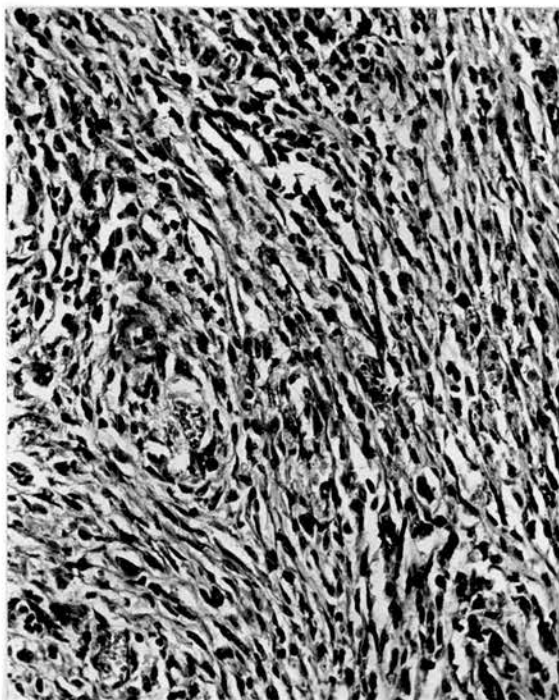


Fig. 56

x 150

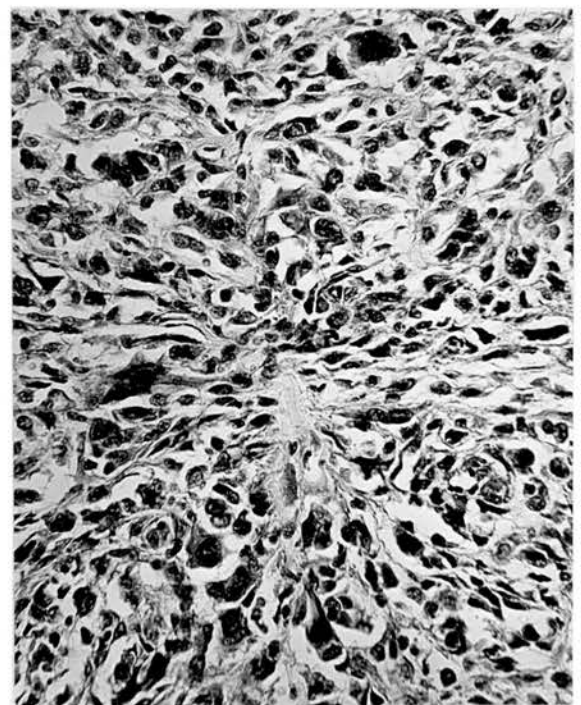


Fig. 57.

x 225.

Case 12.

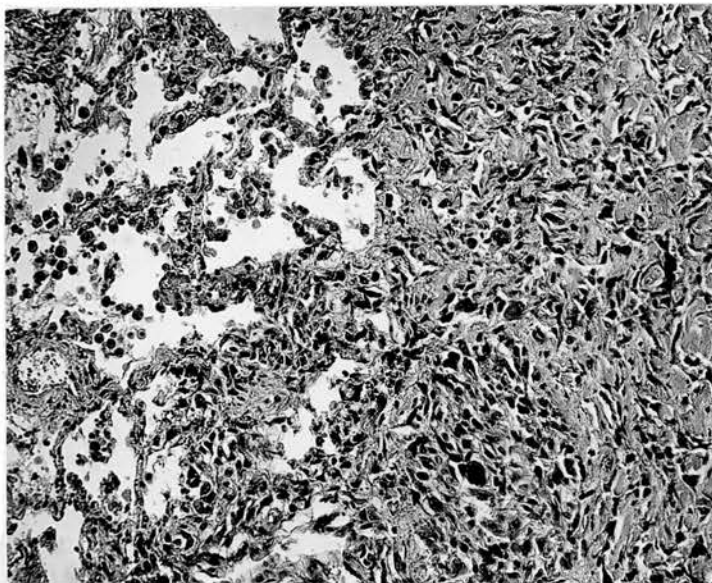


Fig. 58.

x 100.

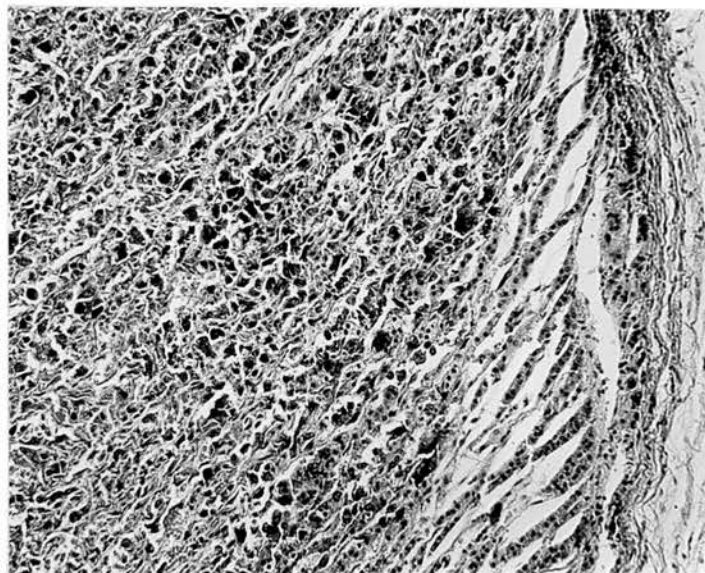


Fig. 59.

x 100.

Case 13.



Fig. 60

x13

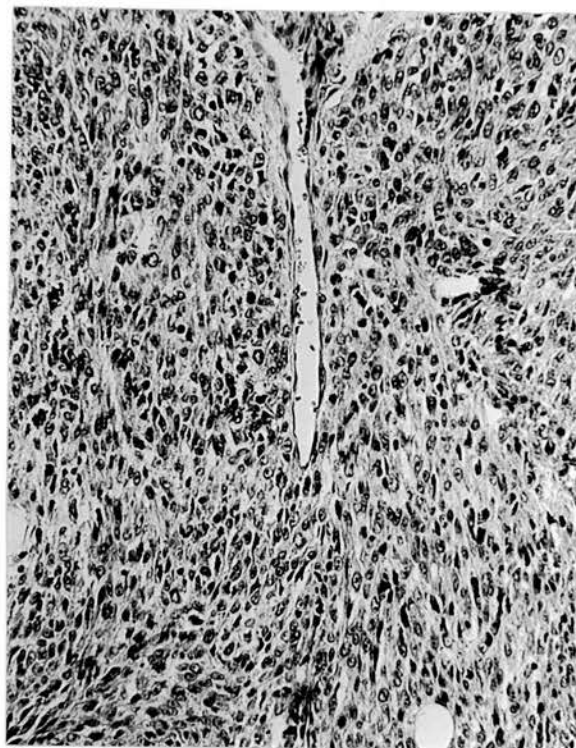


Fig. 61.

x150.



Fig. 62.

x80.

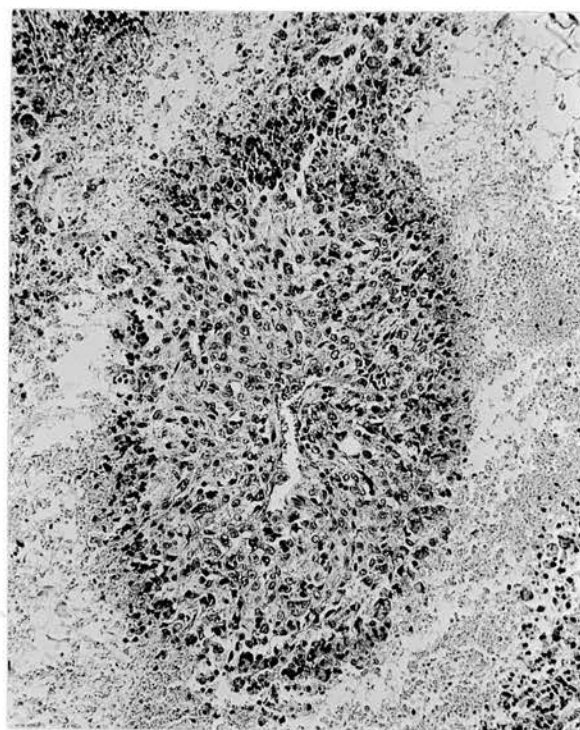


Fig. 63.

x100.

Case 14.



Fig. 64.

x50

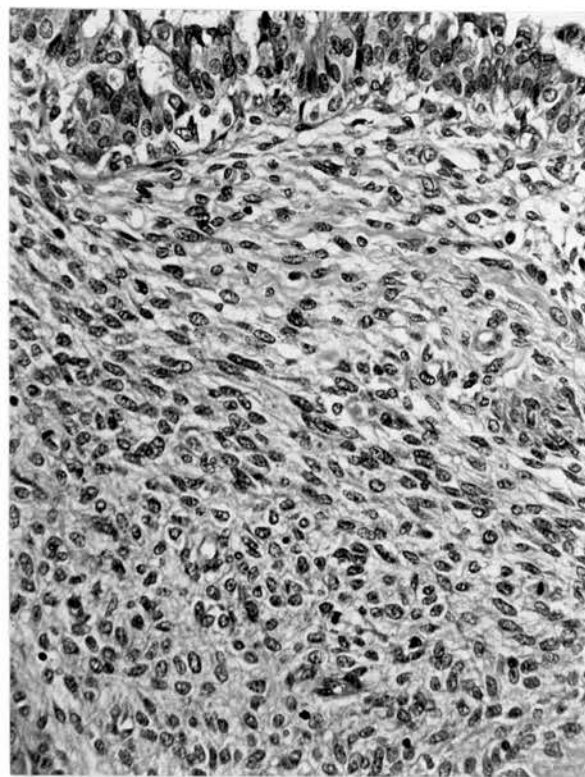


Fig. 65

x250

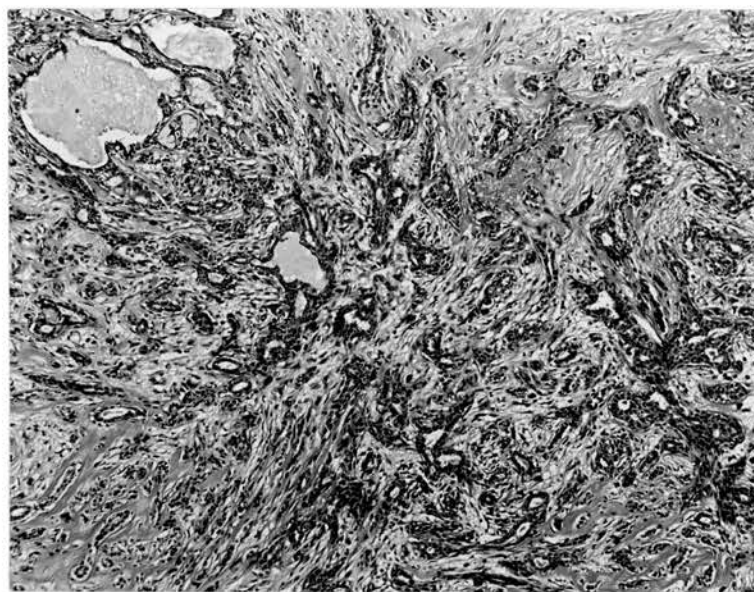


Fig. 66

x70.

Case 15.

S.110.

History: The patient aged 45 years of age had known of a tumour for 6 years. It had enlarged rapidly during the last 2 months but was painless.

Examination showed a very large tumour which suggested a fibroadenoma approaching the skin. A simple mastectomy was done.

Histology: Tissue for examination was sent in 3 pieces. It shows an intracanalicular fibroadenoma with considerable stromal activity of myxoid type in some areas (fig. 67).

Five years later the tumour recurred as a very vascular myxomatous structure (fig. 68) and a radical operation was done; the nodes were found negative. Other areas were closely cellular with round and spindle cells (fig. 69) and scattered small fat cells. Five months later there was a fungating second recurrence (fig. 70) which showed a more typical spindle-celled fibrosarcoma with numerous small vacuoles suggestive again of some lipomatous elements (fig. 71). Death occurred 10 months later, 5 years 10 months after the initial operation.

This case is instructive with the long pre-examination history, the long interval between removal of the tumour and the first recurrence and the successive variation of histological structure.

Case 15

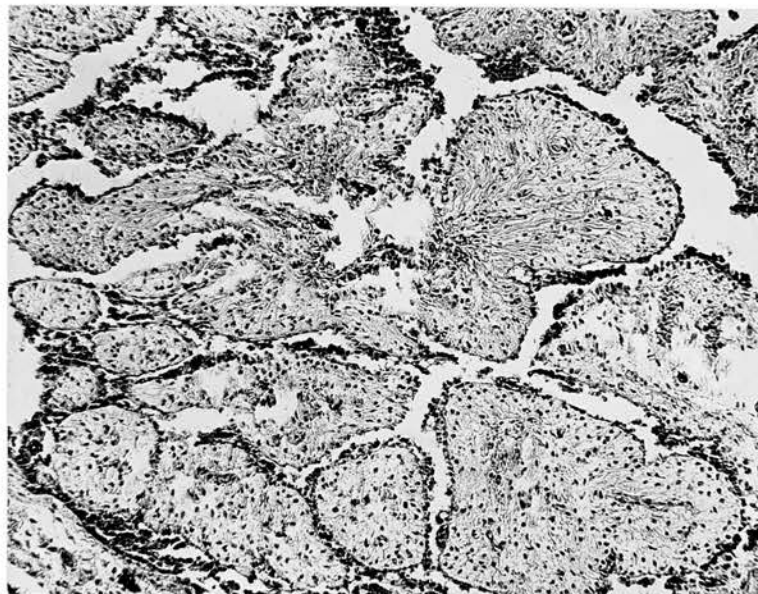


Fig. 67.

×100

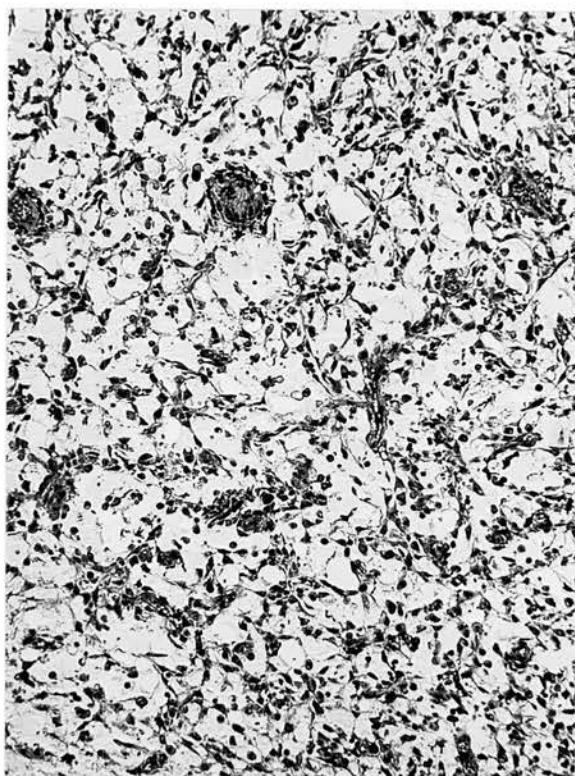


Fig. 68

×100

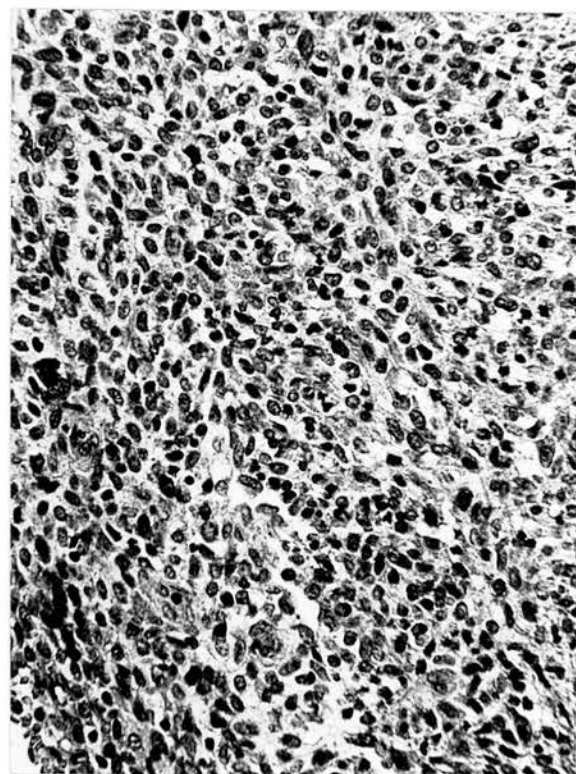


Fig. 69.

×300

Case 15

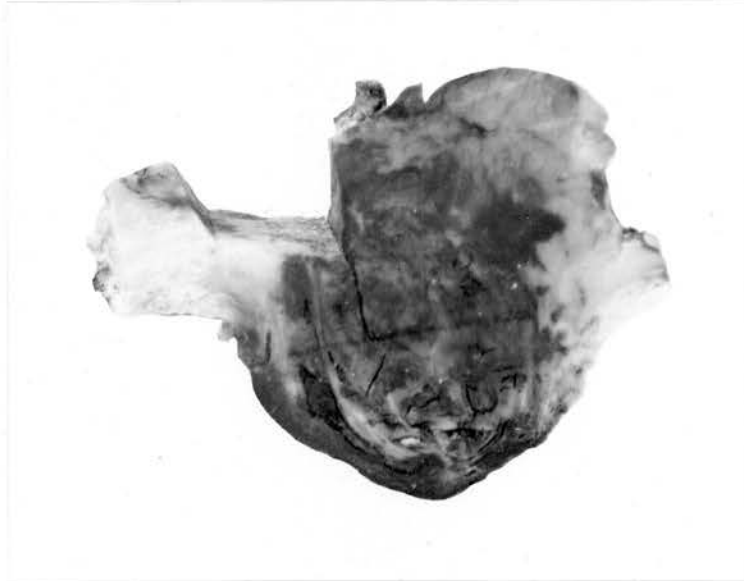


Fig 70

x 1

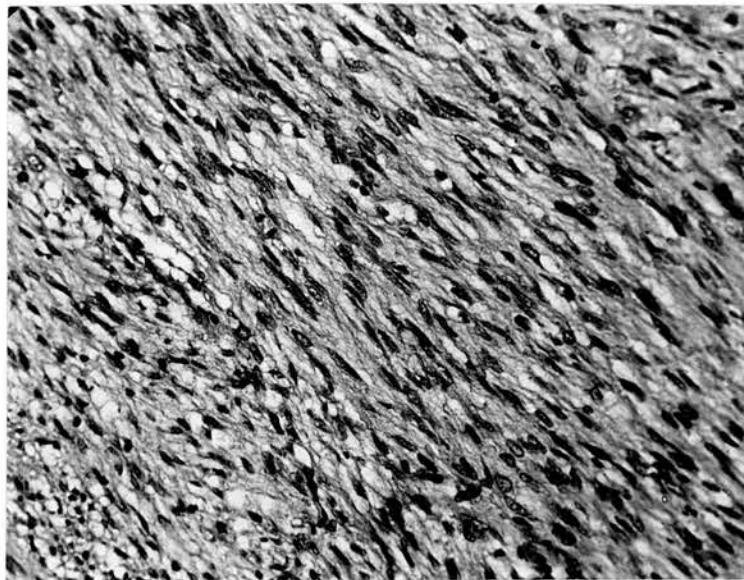


Fig. 71.

x 225.

Case 16.

B.25.

A tumour cut as a whole breast section without clinical data (fig. 72).

Histology: A characteristic giant cystic and malignant fibroadenoma - "cystosarcoma phyllodes" - filling half the breast (a horizontal slice of tissue had been removed). It shows generalized polypoid masses of malignant stroma with inactive epithelial covering and a few small ducts. There is little formation of a capsule and early infiltration is found at several areas of the periphery. The fibrosarcomatous structure shows round and polygonal cells in some parts (fig. 73), in others a closely spindle-cell tissue (fig. 74). Both types show scattered giant cells and considerable mitotic activity.

The benign counterpart of this tumour, a large cystic fibroadenoma in a woman aged 52 is shown in fig. 75, also a whole breast section.

Both tumours were treated by simple mastectomy; the malignant one was presumably without palpable axillary involvement.

The following cases 17 - 26 are not illustrated.

Case 17.

S.24.

History: The patient was aged 59 years. A radical amputation had been done 8 months before examination here and reported as tuberculous. Only two pieces of tissue were received.

Histology: A much infected ulcerated and fungating tumour of spindle-celled fasciculated structure with the malignant cells concentrated round numerous blood vessels. There were many mitotic figures and slight pleomorphism but no mammary gland elements were found. This is a fibrosarcoma but without evidence of tuberculosis.

Case 16

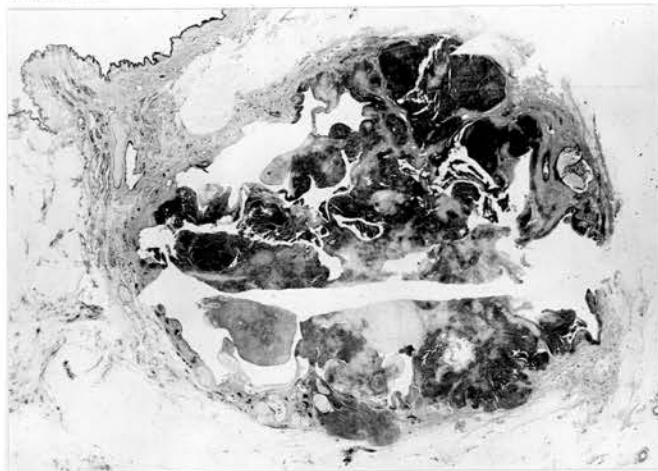


Fig. 72.

x 1.

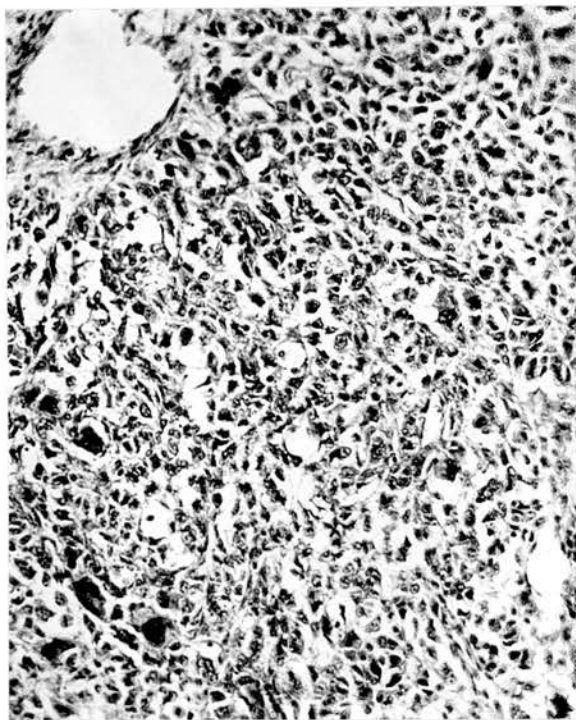


Fig. 73.

x 110.

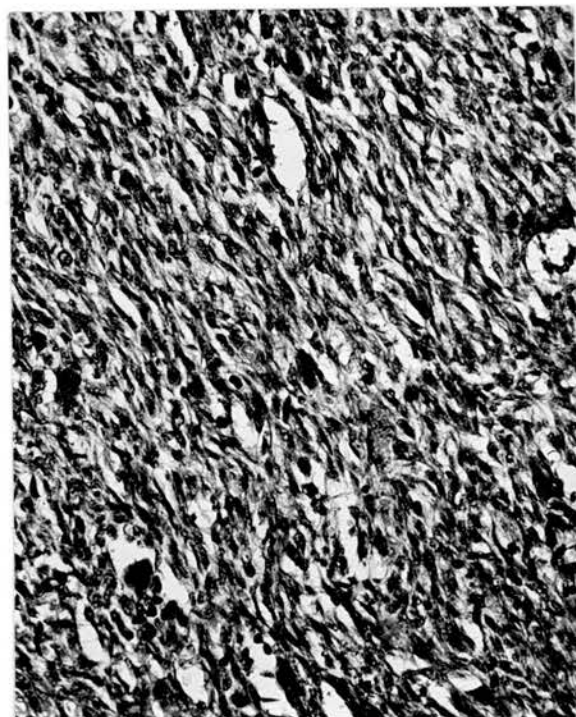


Fig. 74.

x 125



Fig. 75

x 2/3.

Case 18.

S.91.

The patient aged 43 had a tumour excised locally.

Examination showed an ovoid encapsulated tumour 4 x 3 x 2.5 cm. with some fixation to the pectoral fascia. This is a fibrosarcoma of high malignancy infiltrating the pectoral fascia with early invasion of the underlying muscle, but elsewhere showing a defined periphery. Some areas are very pleomorphic with monstrous and multinucleated cells, haemorrhage and haemosiderin deposit. No later note.

Case 19.

S.90.

No clinical notes were sent but the tumour was a spherical mass about 5 cm. in diameter, apparently encapsulated. It had been removed by radical mastectomy from a patient aged 62.

Histology: A myxosarcoma of relatively low grade malignancy arising in the stroma of an intracanalicular fibroadenoma with embedded small ducts. There was much degeneration and haemorrhage towards the centre of the tumour. The cellular perivascular strands of tumour are separated by malignant myxomatous tissue. Both show considerable mitotic activity. No later note.

Case 20.

S.52.

History: The patient was aged 37. Three weeks after the tumour was first noticed, during which time it had been growing rapidly, it was locally excised. It was reported a sarcoma and a radical operation was done as X-rays showed no evidence of pulmonary deposits.

Histology: There was no capsule though the tumour was demarcated against the surrounding corpus mammae. Mammary gland elements were scattered in the malignant stroma which is mainly fibroblastic but with considerable pleomorphism and numerous

mitotic figures. It suggests origin as a pericanalicular fibroadenoma. The patient is alive and well 4 years 9 months after operation.

Case 21.

S.116.

History: The patient aged 71 years noticed a gradually increasing lump in the breast for 8 months.

Examination showed on transection a soft necrotic malignant tumour, greyish in colour with haemorrhages and a defined periphery.

Histology: A fibrosarcoma with no epithelial elements. The tumour tissue shows interlacing bands of spindle-cells of varying malignancy. There are numerous fine capillaries and many dilated congested blood vessels, the walls of which are formed by tumour growth (compare fig. 24). Appearances suggest histogenesis of a fibrosarcoma from a fibroadenoma (compare figs. 12, 13 and 146) with a fibromatous intermediate phase.

Case 22.

S.139.

History: The patient aged 78 years had noticed the tumour for 6 months. The skin was puckered over the tumour which was ill-defined. No nodes were palpable and a simple mastectomy was done.

Examination: The tumour was 4 cm. in diameter, rather hard and suggested carcinoma.

Histology: Fibrosarcoma with considerable haemorrhage, necrosis and calcific deposit. It shows interweaving strands of fairly uniform spindle-cells with numerous mitotic figures in the more densely cellular areas. The tissue is very vascular with numerous capillaries "cuffed" by proliferating tumour cells. There is no trace of any fibroadenomatous structure.

Case 23.

S.177.

History: The patient aged 64 years had noticed swelling of one breast for several months.

Examination: A fatty breast, removed by radical operation contained a large firm tumour 6 cm. in the greatest diameter and on transection was soft, lobulated and fairly well defined, but with smaller subsidiary nodules. Some small nodes in the axillary fat did not look malignant.

Histology: A fibrosarcoma with strands and whorls of spindle-cells and considerable mitotic activity. No epithelial elements were identified and the axillary nodes were negative. The patient was alive 6 years 7 months after operation, but senile.

Case 24.

S.29.

History: The patient aged 53 had noticed a mammary tumour, gradually increasing in size for 6 years. It was latterly painful.

Examination: A large spherical nodular tumour had been diagnosed as cystosarcoma. There was no nipple retraction, no palpable axillary nodes but some bluish discolouration of the skin with dilated superficial veins.

Histology: A fibrosarcoma. Some fibroadenomatous structure is still evident but cellular areas of spindle cells with no glandular tissue show moderate mitotic activity. No later note.

Case 25.

S.22.

History: No clinical data sent except "a good example of a fibrosarcoma with ulceration of the overlying skin".

Histology: The periphery is well defined in the area sent. Much of the tumour shows interweaving strands of malignant spindle-cells but also numerous scattered cells of monstrous type and many mitotic figures. This is a fibrosarcoma.

Case 26.

S.169.

History: A patient aged 69 said she knew of a tumour in the breast for 40 years.

Examination showed an enormous lobulated mass clinically regarded as a "Brodie's sero-cystic tumour". There were no palpable axillary nodes.

Histology: A fibrosarcoma with some remaining fibroadenomatous structure of myxoid and loosely fibroblastic type. Both types showed many mitotic figures. There is great congestion (history of trauma) and some vessels have no endothelial lining. No later note after mastectomy.

Cases 27 - 33 are tabulated only.

OSTEOSARCOMA AND CHONDROSARCOMA

Cases 34 - 51. Figs. 76 - 152.

Osteosarcoma and Chondrosarcoma

Before metaplasia was an accepted phenomenon, various attempts were made, mainly in the earlier German literature, to explain the presence of bone and/or cartilage in the breast as congenitally misplaced tissues from some neighbouring normal bone, sternum, ribs and clavicle being the most usual explanations (Stilling 1881, Arnold 1887, Hüter-Karrenstein 1906, Kreibitz 1925).

In an earlier study of mammary sarcoma, bone or cartilage or both were found in 29 of 92 tumours (Dawson 1960). More examples for further study have since been available. The structure in this mammary tumour type varies greatly; usually there is osteoid tissue with some calcification and possibly differentiation into mature bone suggested by a gritty feel on transection and cartilage possibly also identifiable macroscopically. Ossification and chondrofication are apparently slow processes, as most cases occur in middle-aged or elderly subjects. Bone in my material is a more frequent metaplastic finding than cartilage in mammary sarcomas but both have a bad prognosis. A purely osteoclastic structure was not found in any of this series although numerous osteoclasts were present in many examples in association with bone and cartilage. As in almost all other mammary sarcomas there was no lymph node involvement in this group.

As bone formation may be found in metastatic growth from primary sarcomas of bone or of some soft tissues, this possibility needs elimination in the diagnosis of ossifying and chondroforming mammary tumours.

Clinically a very hard tumour in the breast usually indicates osteoid or bony metaplasia, possibly in a sarcoma. Occasionally however non-neoplastic bone is formed in the stroma of mammary carcinoma (fig. 153) and even in the associated malignant lymph nodes (fig. 154).

Cartilage may be found in the stroma of tumours other than mammary, as for example, in salivary gland tumours, when its formation might be explained by mucous secretion from the glandular tissue forming a potential chondromucinous anlage for its development. Fig. 155 shows a malignant salivary gland tumour separated by a zone of hyaline tissue from a cartilaginous area, the identification of which can be demonstrated by P.A.S. staining.

In elderly subjects, fibroadenomas may become partially or wholly hyalinized, sometimes with calcific deposit, a condition which also produces a hard mass in the breast, suggestive of malignancy (figs. 156 & 157).

Bone - Cartilage - Osteoclastoma

| Series | Reference | Age | Duration of tumour. (years). | Type | Nodes | Therapy | Outcome in years. | Metastases |
|--------|-----------|-----|------------------------------------|------------------------------------|-------|--------------------------------------|-----------------------------|-----------------------------------------------------------------------------------|
| 34 | S.4. | 43 | ? | Bony with osteoclasts | - | Radical mastectomy | Alive 3 ⁷ /12 | - |
| 35 | S.53. | 65 | 5/52 | Chondrosarcoma | - | Simple mastectomy | 2 Recurrences Died 10/12 | - |
| 36 | S.18. | 62 | 2/12 | Osteosarcoma | - | Biopsy and radical mastectomy | Died 13/12 | Lung & skin. |
| 37 | S.51. | 49 | Short time | Osteosarcoma from fibroadenoma. | - | Radical mastectomy | Died 2 ¹ /12 | Nose, Lungs Mediastinum Tibia & Rib. |
| 38 | S.153 | 61 | 15. | Osteochondroma + carcinoma. | - | Radical mastectomy | Died | - |
| 39 | 964. | 62 | 2/12. | Osteosarcoma | - | Local excision | Died 2 ¹⁰ /12 | Lung. |
| 40 | S.168 | 64 | 3-4 yrs. | Osteosarcoma. | - | Simple mastectomy | Died 9/12. | Mediastinum. Pleura. Pericardium. Cervical vertebrae. Lung. Heart. |
| 41 | S.167 | 32 | (Removed post Lactation). | Chondrosarcoma | - | Local excision | Alive 8. | - |
| 42 | 758 | 70 | Many yrs. | Bony. | - | ? | ? | - |
| 43 | S.27 | 59 | 18/12 | Osteoid | - | Radical mastectomy | Died 3 ⁴ /12 | - |
| 44 | S.141 | 56 | 21 yrs. now enlarging | Osteosarcoma | - | Mastectomy | Died. | - |
| 45 | 1137 | ? | ? | Chondrosarcoma | - | Local excision | ? | - |
| 46 | 1402 | ? | ? | Osteosarcoma | - | Radical mastectomy | ? | - |
| 47 | S.147 | 57 | 2/12 | Chondrosarcoma | - | Radical mastectomy + irradiation. | Died 1 ¹⁰ /12 | - |
| 48 | S.17 | 56 | 2. | Fibrochondrosarcoma | - | Simple mastectomy | ? | - |
| 49 | S.165 | 59 | 6/52 | Osteosarcoma | - | Radical mastectomy | Died 1 ¹⁰ /12 | - |
| 50 | S.58 | 50 | ? | Osteosarcoma | - | ? | ? | - |
| 51 | S. 97. | 54 | ? | Osteoclastoma | - | Radical mastectomy | ? | - |

Case 34.

S.4.

History: The patient aged 43 had a large tumour of unknown duration.

Examination: The tumour was defined, hard, but mobile and suggested a carcinoma. A radical mastectomy revealed no axillary nodes.

Histology: Transection showed a very fatty breast containing a tumour which resembled a giant cell tumour of bone (fig. 76), with many cavities filled with fresh blood (fig. 77 actual size in colour). All areas show bone formation as trabeculae (fig. 78) or diffuse (fig. 79) and numerous osteoclasts mixed with single or multinucleated large tumour cells (figs. 80 & 81). The patient was alive and well 3 years 7 months after but later was lost sight of.

Case 35.

S.53.

History: The patient aged 65 years had noticed a lump in the left breast for only 5 weeks. There was no pain or discharge or history of injury. It suddenly grew very rapidly to this enormous size. She was urged by her family to see her doctor, who referred her at once to hospital.

Examination showed a huge tumour (figs. 82 & 83), soft and haemorrhagic and fixed to muscle, diagnosed "probably sarcoma", with no palpable nodes. The skin was tightly stretched over the tumour with flattening of the nipple. The condition was quite beyond radiotherapy. At operation a pint of serous fluids was evacuated. The tumour tissue looked bluish on transection and suggested a chondro-mucinous growth.

Histology: There are many areas of malignant cartilage and also a diffuse growth of small-cell undifferentiated sarcoma (figs. 84 & 85). The periphery is more fibroblastic but without capsule. In areas it shows a lobulated structure with polypoid masses denuded of epithelium, suggesting histogenesis as an intracanalicular fibroadenoma. In other areas there is great vascularity with parallel capillaries surrounded by malignant cells (fig. 87). Methylene blue staining emphasizes the numerous mitotic figures in the cartilaginous areas and elsewhere (figs. 84, 85 and 86). There were two recurrences in the tumour area and the patient died 10 months after operation.

Case 34.

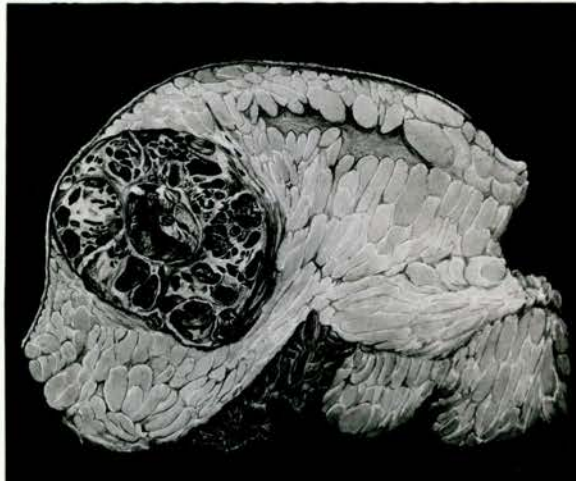


Fig. 76.

x 1/3.

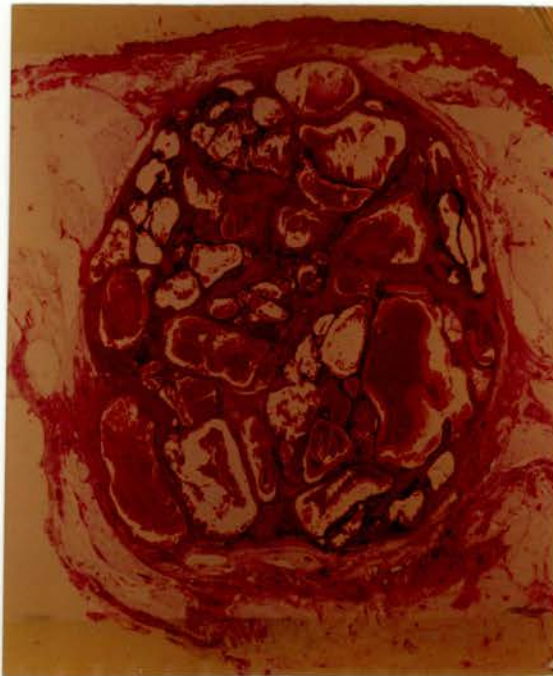


Fig. 77.

x1.

Case 34.



Fig. 78.

x 70.

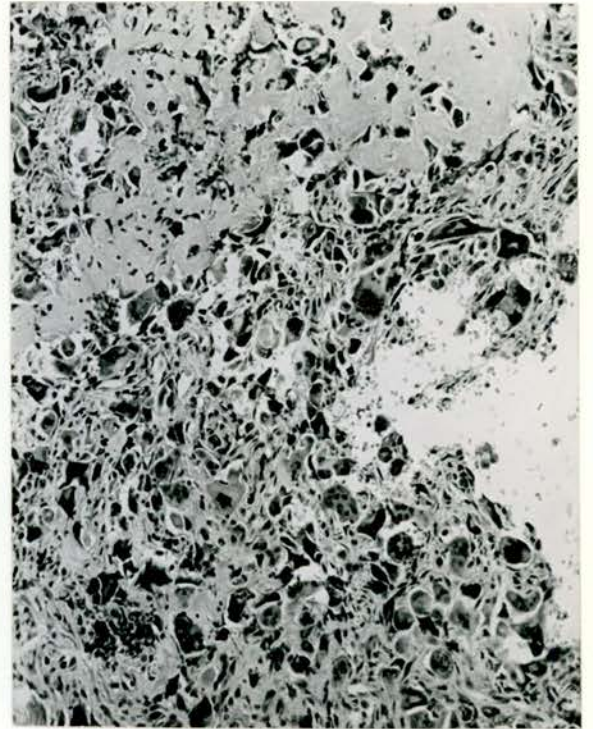


Fig. 79.

x 140.

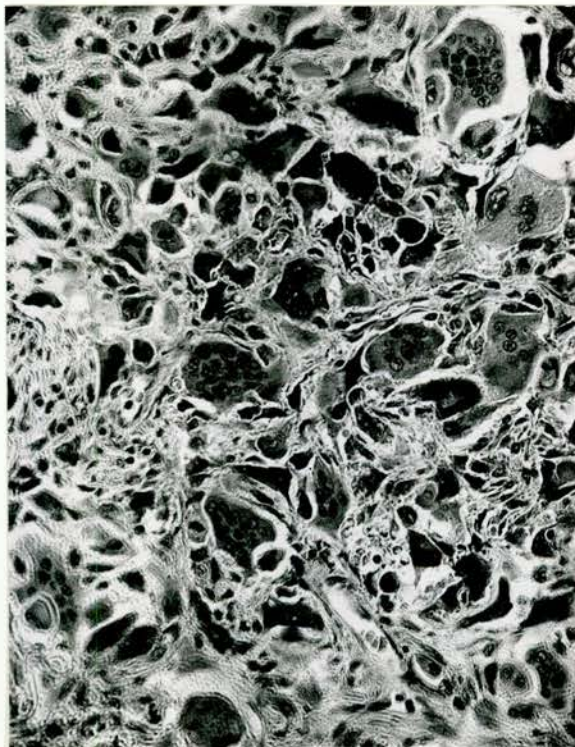


Fig. 80.

x 250.

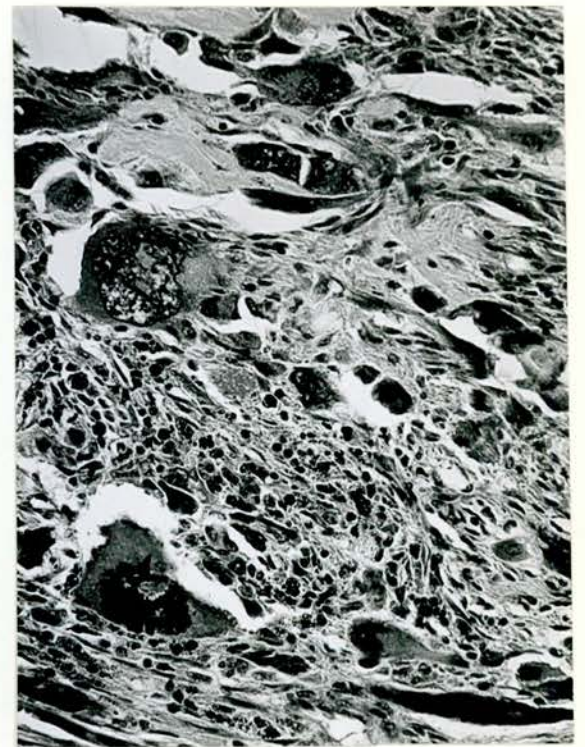


Fig. 81.

x 250.

Case 35.



Fig. 82.



Fig. 83.

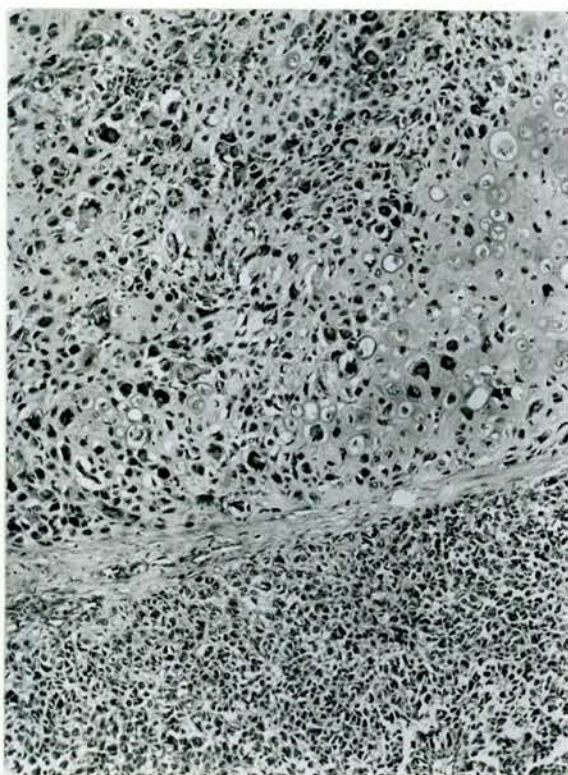


Fig. 84.

x70.

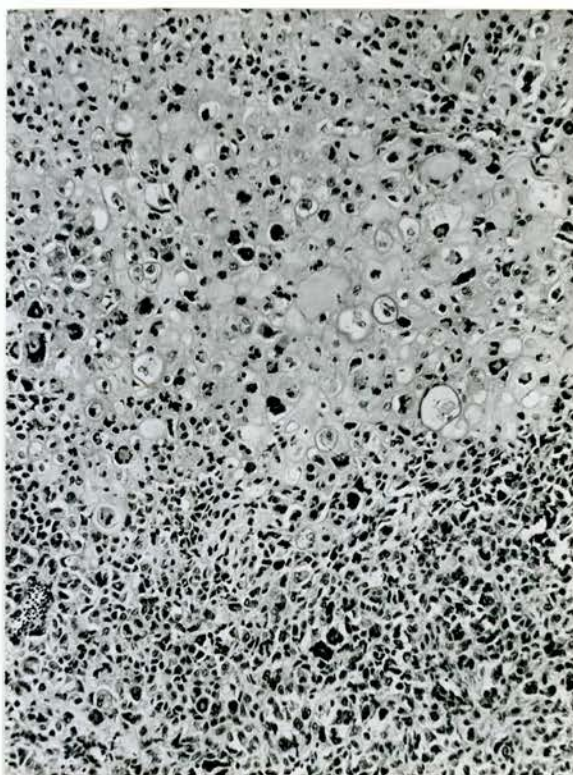


Fig. 85.

x100.

Case 35.

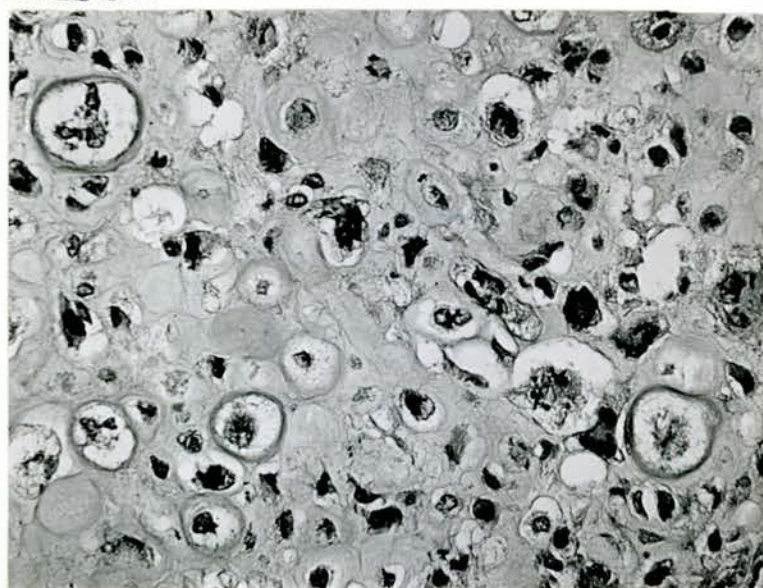


Fig. 86.

x 250.

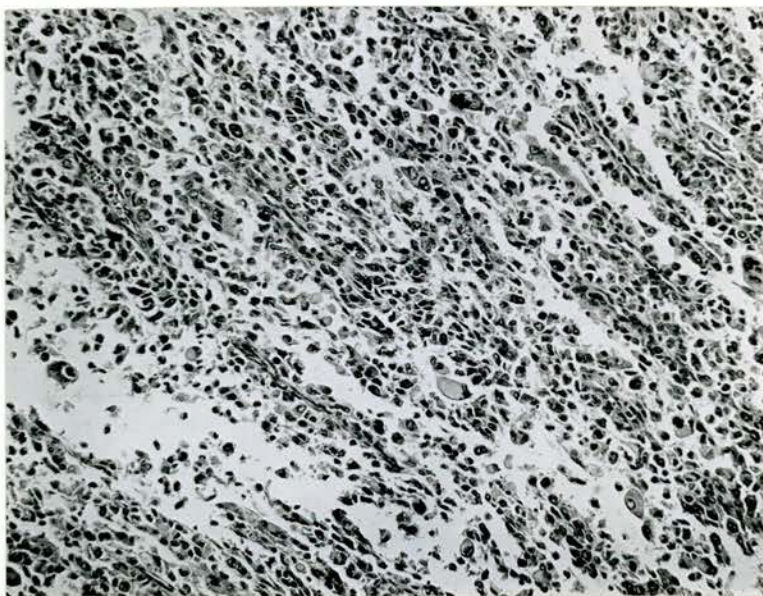


Fig. 87.

x 100.

Case 36.

S.18.

History: The patient aged 62 had known of the tumour for only 2 months but it was large and approaching the skin.

Examination: A small biopsy sent initially was equivocal but contained some bone. A radical mastectomy followed and the defined hard tumour (fig. 88) was sent, cut parallel to the skin surface. It had to be decalcified for microscopy. It recurred as a much larger growth with invasion of pectoral muscle and the appearance of a giant cell tumour of bone (fig. 89).

Histology: Many areas of both primary and recurrent tumour were examined. The primary tissue shows a diffuse membranous bone formation, with patchy proliferating osteoblasts and comparatively few osteoclasts (figs. 90 & 91). The recurrent larger tumour had a cystic haemorrhagic appearance with a more cellular osteoblast and osteoclast structure. The dilated blood vessels contain many malignant cells mixed with the blood (figs. 92 & 93).

The patient died 13 months after the initial biopsy with lungs and skin extensively invaded. Autopsy tissue was not available for examination.

Case 37.

S.51.

History: The patient aged 49 had noticed a tumour in the breast for only a short time.

Examination: The swelling in the upper outer quadrant suggested a carcinoma (fig. 94) and a radical mastectomy was done. The axillary nodes were not invaded. One year 11 months later she developed a painful swelling of the nose which was thought to be inflammatory (fig. 101) but incision found no pus and examination of a small biopsy showed tumour.

Histology: Some areas show quiescent or atrophic intracanalicular fibroadenoma with some cellular fibromatous activity (fig. 95). Much of the tumour shows a fibroblastic matrix in which are bony trabeculae, osteoclasts (figs. 96 & 97), cavities with blood

similar to a malignant giant cell tumour (fig. 98), small areas of cartilage (fig. 99) and foci of cholesterol crystal clefts (fig. 100). The nasal biopsy shows active sarcoma with numerous abnormal mitotic figures but no bone or cartilage (fig. 102).

The patient died 2 years 1 month after the mastectomy. X-ray had revealed multiple metastases in lungs, mediastinum, tibia and a rib. No lymph nodes were palpable in any area.

This is a blood-borne dissemination characteristic of sarcoma.

Case 38.

S.153.

History: The patient aged 61 had noticed a lump in the breast 15 years previously. Her doctor gave her "something to put on it". The breast meanwhile had not increased in size but during the week before examination it had become rather painful.

Examination: There was a large irregular swelling in the lower outer quadrant of the breast, fixed to the skin and to the deeper tissues. No lymph nodes could be felt in the axilla but the tumour appeared to be a carcinoma and a radical mastectomy was done.

Histology: The tissue received shows a great variety of structure. Histogenesis from an intracanalicular fibroadenoma is evident in figs. 103 & 104 which show polypoid stromal masses with bony and cartilaginous metaplasia with osteoclasts, projecting into ducts which have partly lost their epithelial covering. Osteo-chondromatous areas, with osteoblasts and osteoclasts are seen in fig. 107; a chondrosarcomatous area is covered by degenerating epithelium (fig. 108). In the central areas, a cellular haemangiopericytomatous structure (fig. 105) passes into a diffuse malignant spindle-celled tissue with early bony or cartilaginous metaplasia (fig. 106). Most areas show some osteoclasts. An unexpected finding outside the tumour is an infiltrating scirrhus carcinoma (fig. 104); its origin in small ducts is not included in the area shown.

This is a difficult tissue to analyse. The polypoid masses of the fibroadenoma of 15 or more years duration must apparently be considered the initial tumour formation. The haemangiopericytoma tissue could develop in these polyps, passing into a diffusely cellular and undifferentiated tissue with a later metaplasia to bone and cartilage with osteoclasts. Bone and cartilage could also develop directly in the stromal polyps. The carcinoma is coincidental.

Case 36

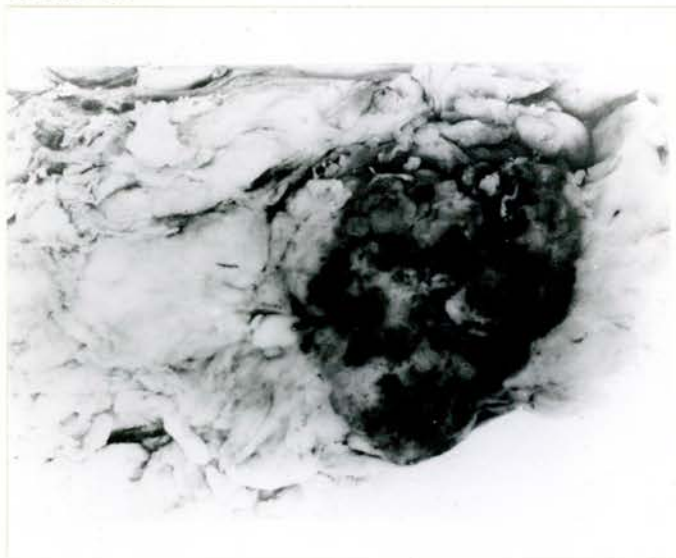


Fig. 88.

x1.

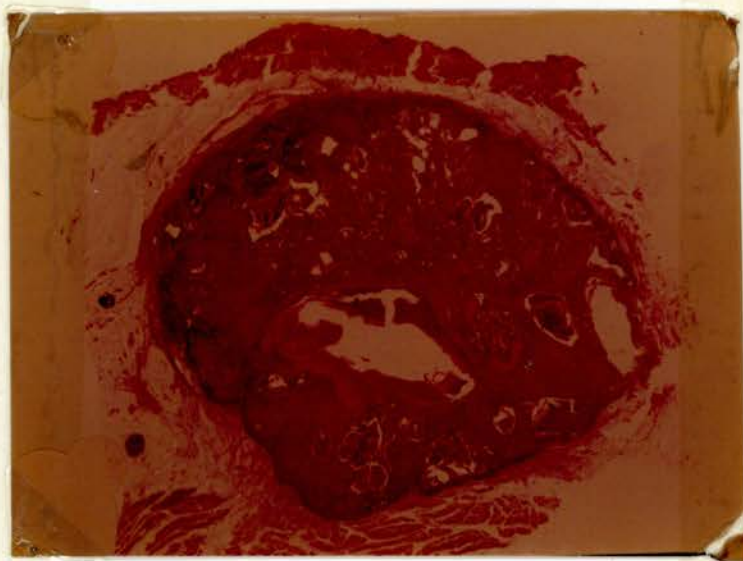


Fig. 89.

x1.

Case 36.

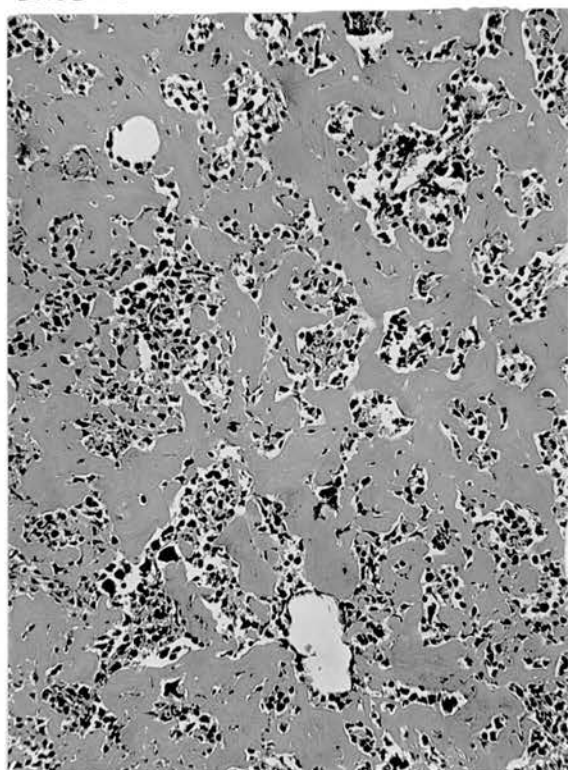


Fig. 90.

x100.

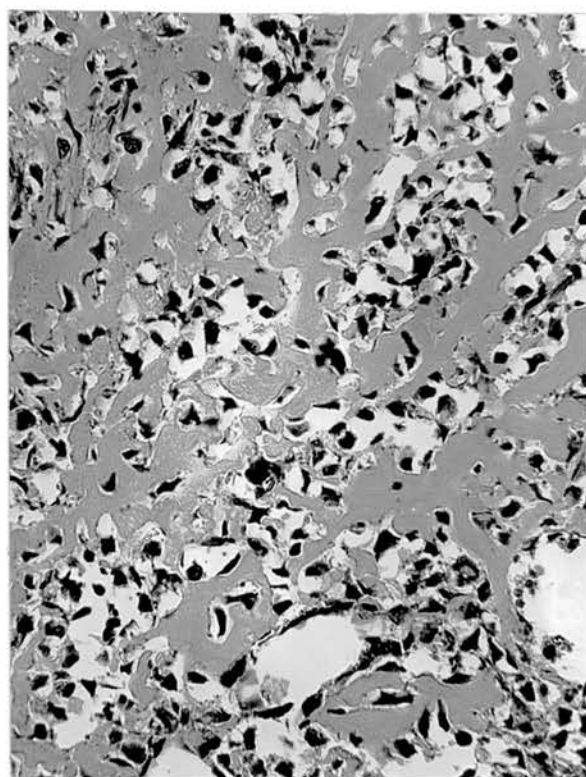


Fig. 91.

x250.

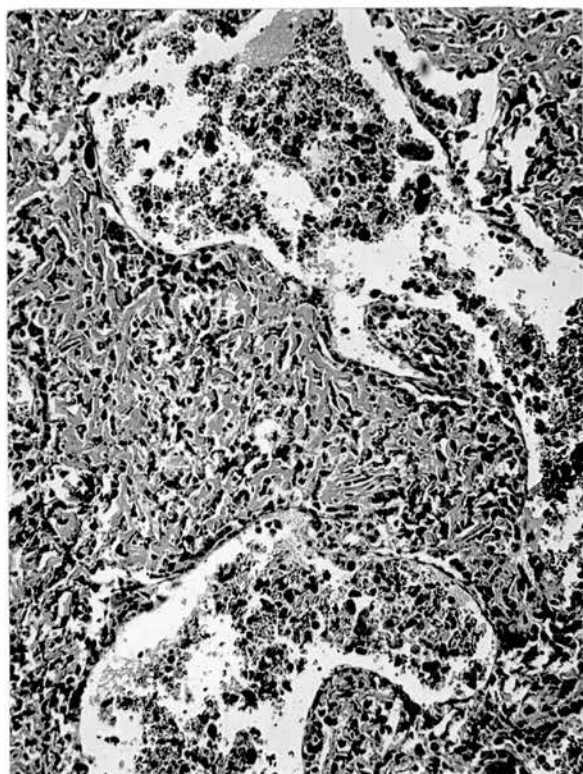


Fig. 92.

x100.

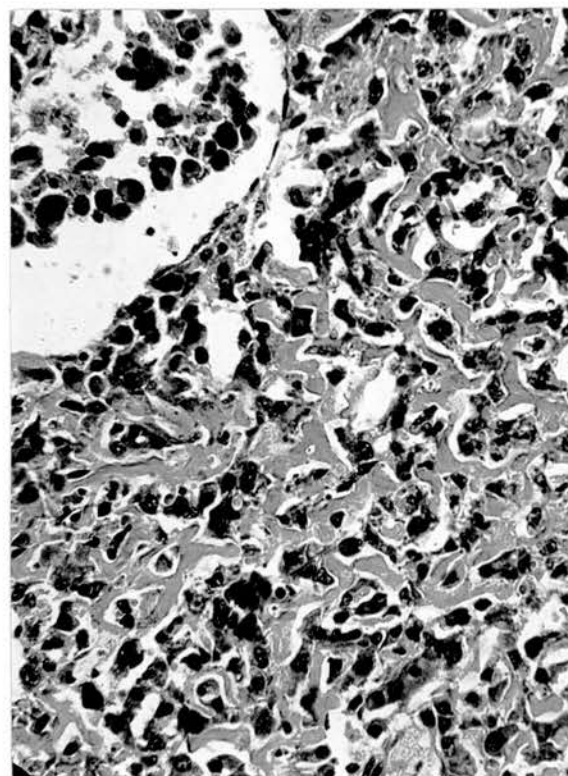


Fig. 93.

x250.

Case 37.



Fig. 94.



Fig. 95.

x10.

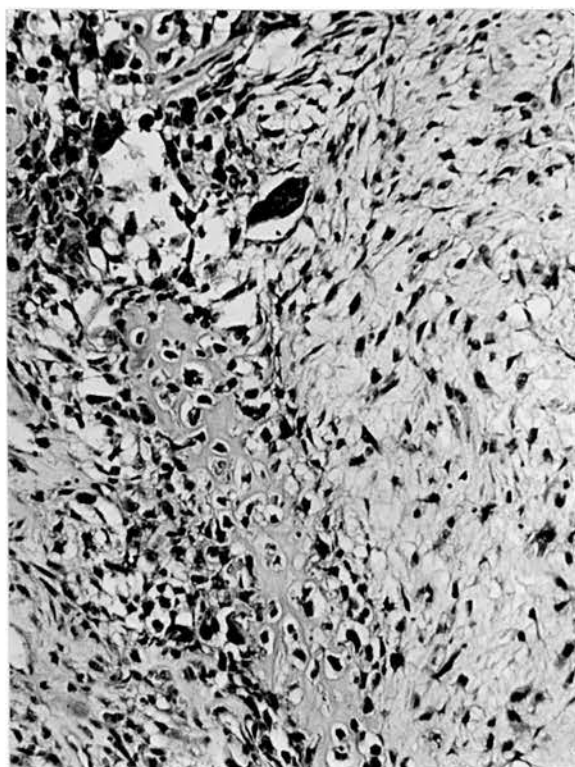


Fig. 96

x150

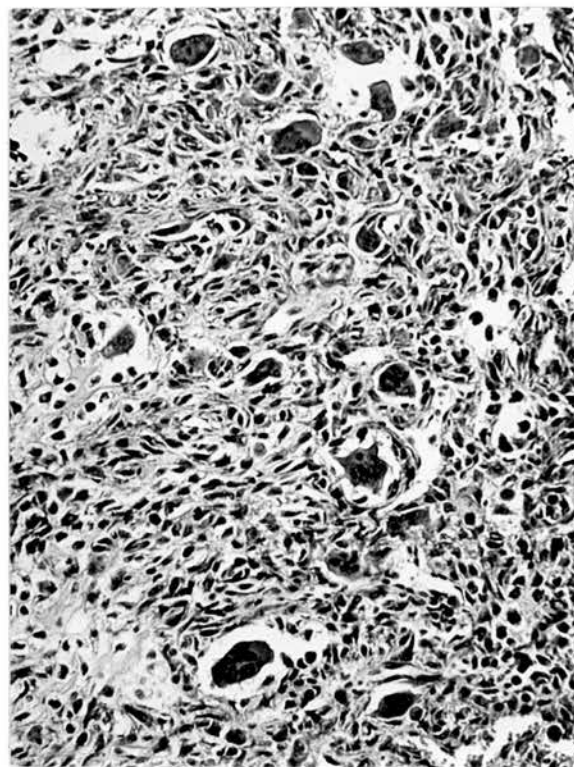


Fig. 97.

x150.

Case 37.

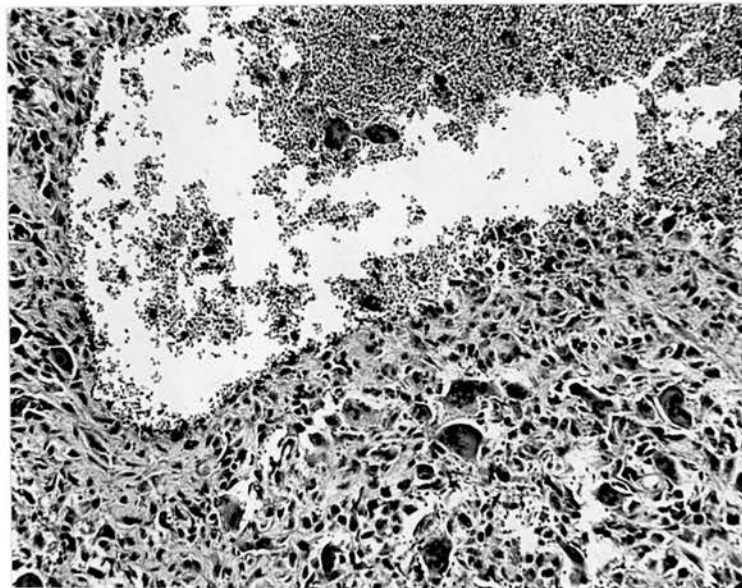


Fig. 98.

x 100.

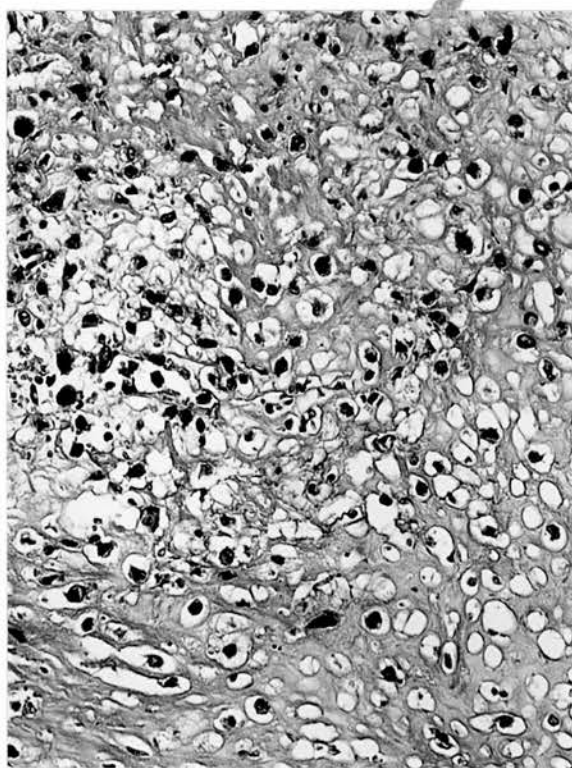


Fig. 99.

x 150

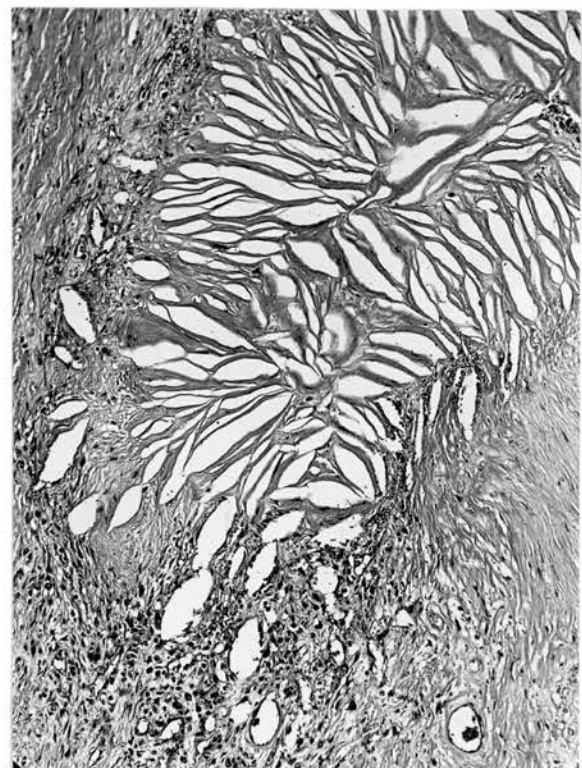


Fig. 100.

x 60.

Case 37.



Fig. 101.

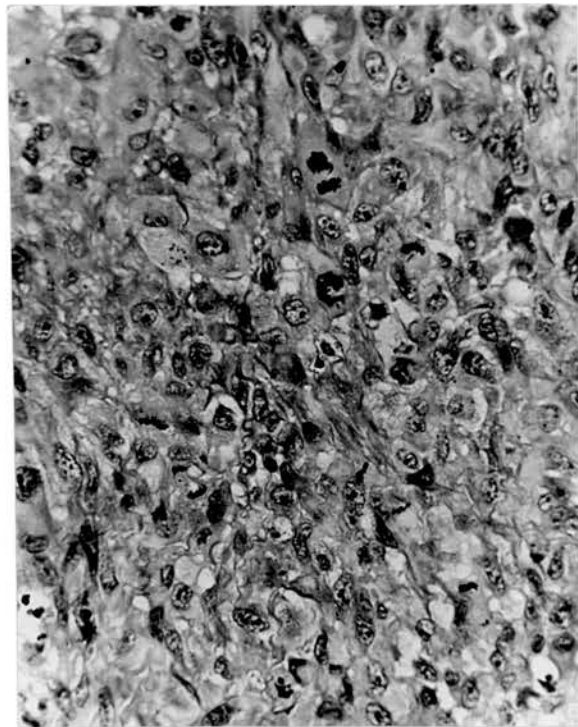


Fig. 102

x200.

Case 38.

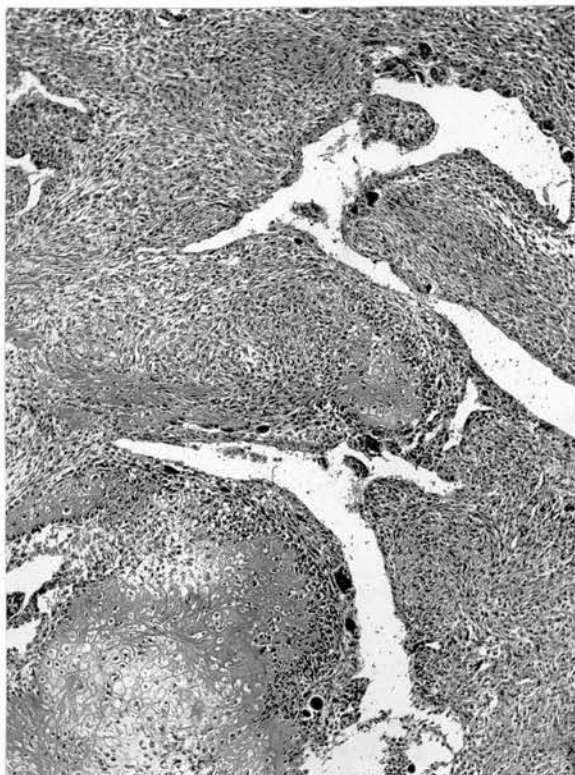


Fig. 103.

x50.

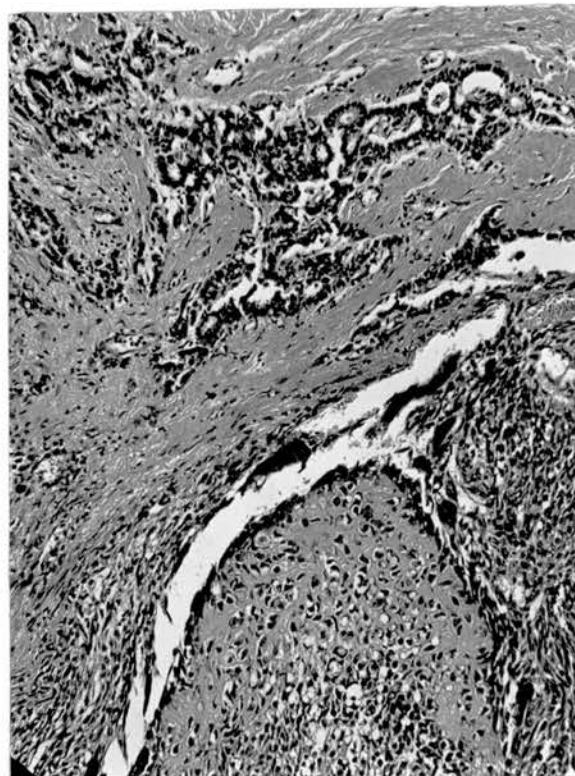


Fig. 104.

x100.

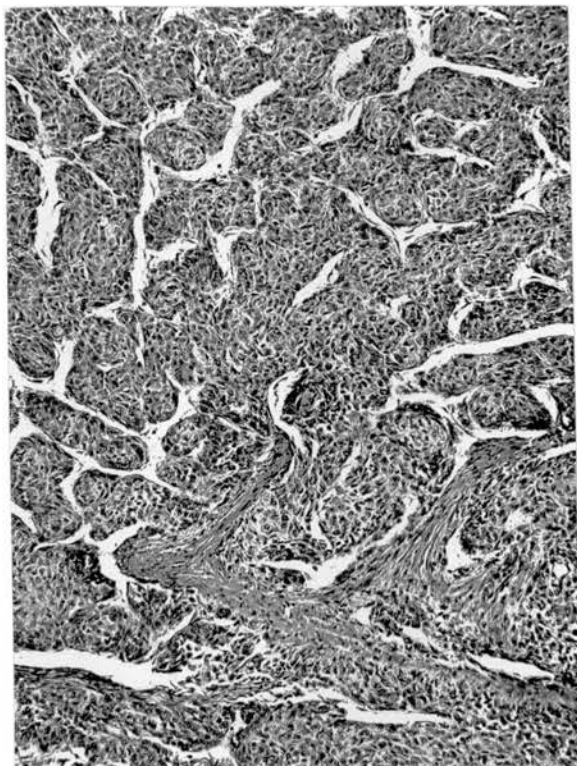


Fig. 105

x100

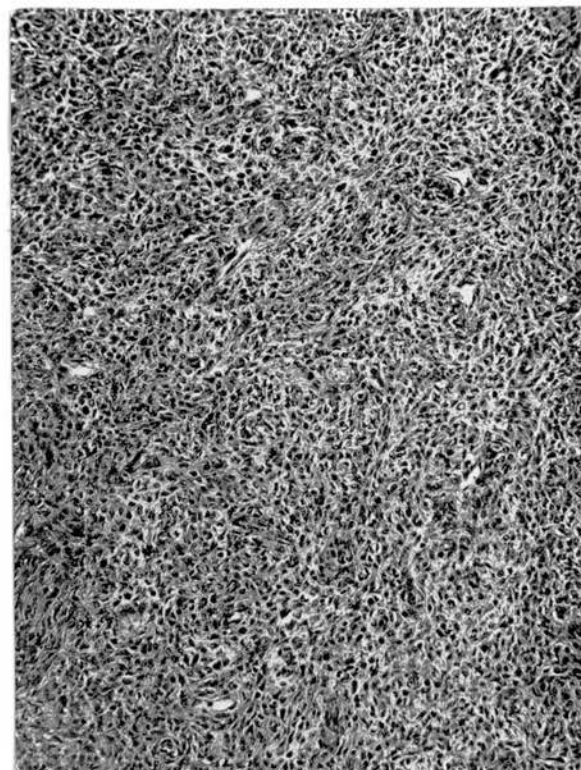


Fig. 106.

x100.

Case 38.

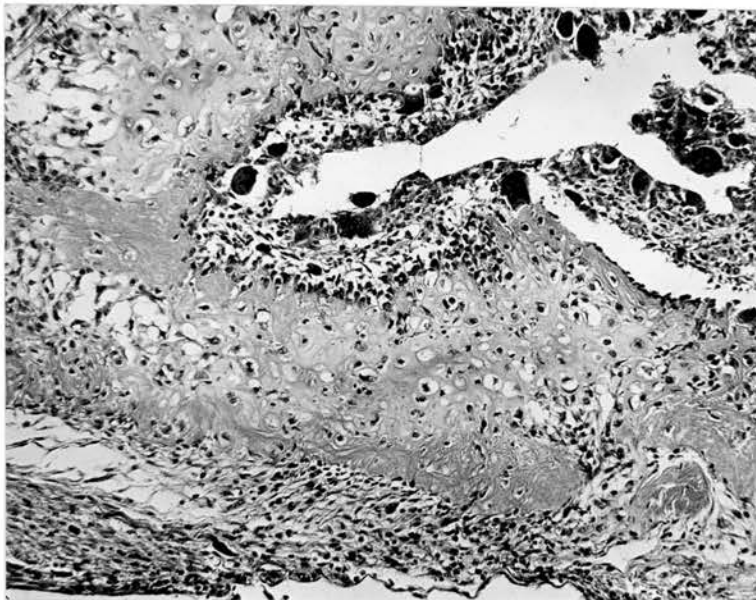


Fig. 107.

x 100.

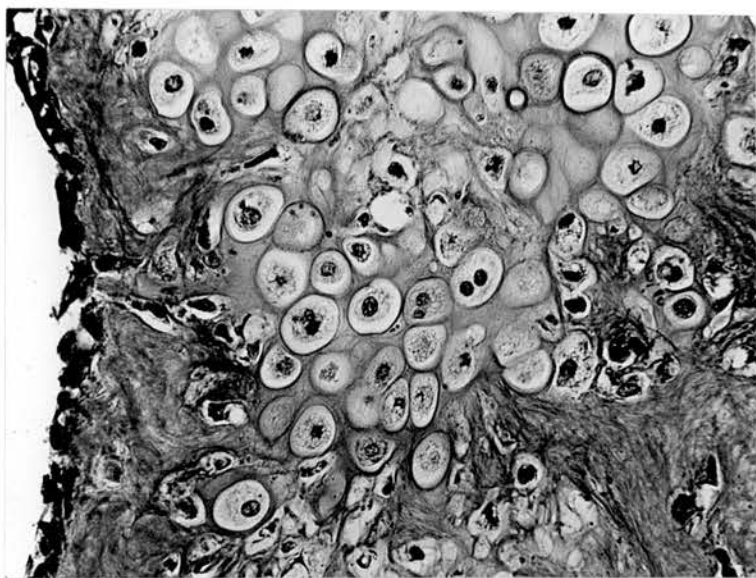


Fig. 108

x 300.

Case 39.

964.

History: The patient aged 62 noticed a lump in the breast for 2 months. She had pulmonary tuberculosis when 16. There was no history of trauma or previous surgery.

Examination showed a very hard mass 5 x 3 x 2 cm. in the upper outer quadrant. Half the tumour area is shown in fig. 109 as a stained section.

Histology: The structure varies considerably but the periphery was fairly well defined. A fibroblastic area with dilated capillaries and scattered osteoclasts is seen in fig. 110. Other areas show osteoid tissue irregularly calcified and very vascular (fig. 111). Fig. 112 shows also a small ill-defined cartilaginous area and at the periphery there is active fibroblastic growth with mitotic activity (fig. 113).

There was considerable discussion with other pathologists about this case. Was it tumour because of its definition and cellularity in some areas? or reactive with vascularity, congestion and calcification though no history of trauma was given?

She remained fairly well for 2 years then developed dyspnoea and chest pain. She was referred to a chest physician who found no obvious secondary involvement but X-rays showed an old healed tuberculous focus together with a new homogeneous opacity in the periphery of the anterior segment of the right upper lobe. There was also hazy streaking running out from the right hilum. She was admitted to hospital but there was rapid deterioration of her condition and she died 2 years 10 months after operation without evidence of local recurrence or of secondaries elsewhere than in the lung. There was no autopsy. There remains some uncertainty as to the cause of death but the mammary tumour seems the more likely explanation than re-activation of the 46 year old tuberculosis.

Case 39.



Fig. 109.

x 5/8.

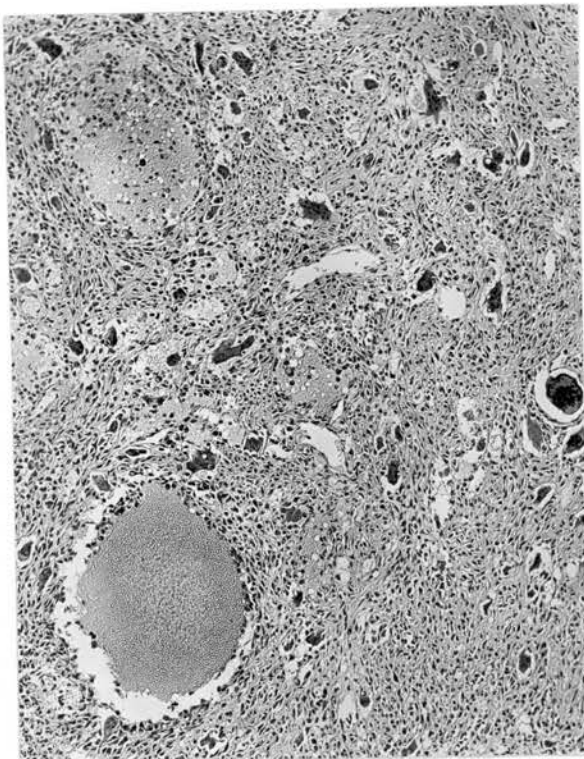


Fig. 110.

x70

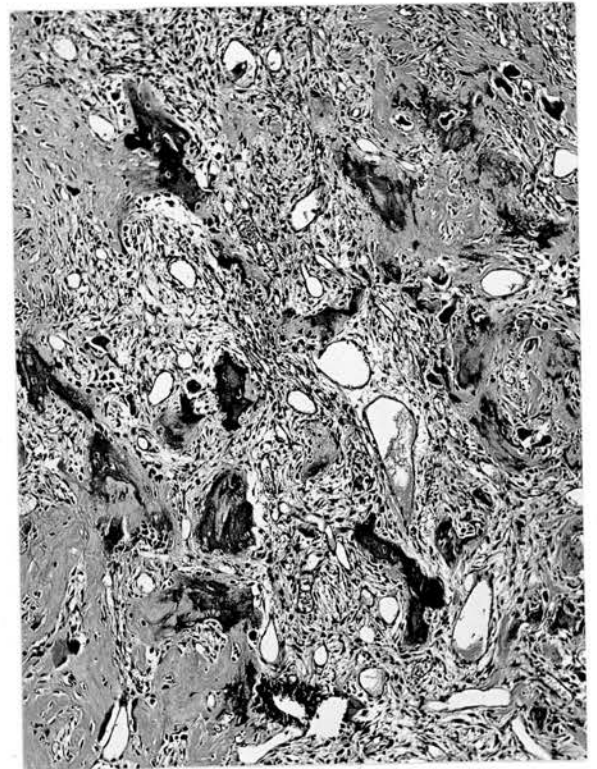


Fig 111.

x70.

Case 39.

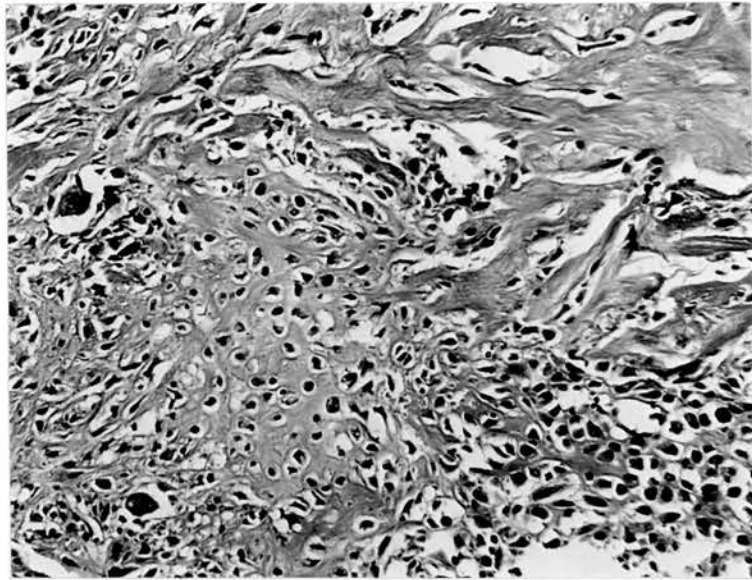


Fig. 112.

x 160.

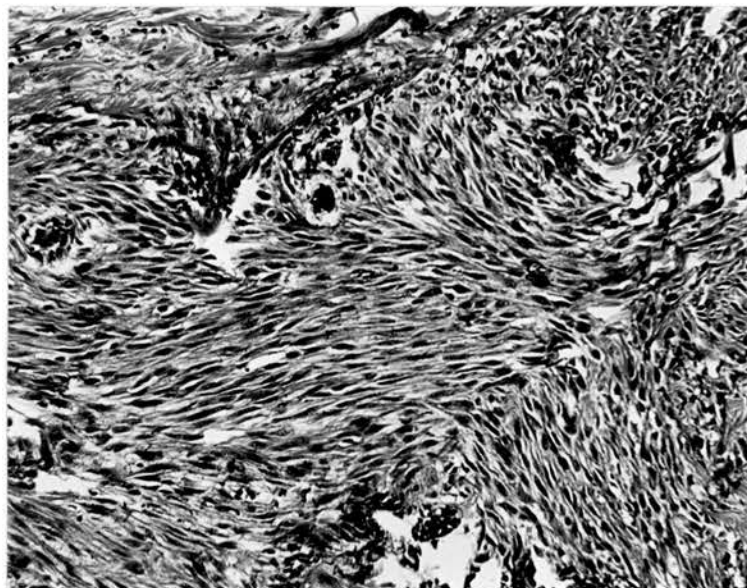


Fig. 113.

x 110.

Case 40.

S.168.

History: The patient aged 64, complained of a gradual enlargement of the left breast during 3 to 4 years.

Examination showed "an enormous Brodie's tumour" i.e. a giant fibroadenoma. The simple mastectomy tissue weighed 2750 gm. There were multiple ulcers and sinuses in the overlying skin. Transection showed a tumour with ill-defined borders of firm hyaline stroma, osseous in one area. There were numerous clefts in the tumour tissue and much necrosis. No normal mammary gland elements were recognizable naked-eye.

Histology shows a varied picture. Some fibroadenomatous areas of the giant benign original tumour are still present (fig. 114), with transition into active fibroblastic tissue (fig. 118) with some residual small ducts. Osteoid tissue is seen at various stages in fig. 115 as narrow fibrillar strands outlined by proliferating osteoblasts with osteoclasts; fig. 116 shows larger rounded osteoid areas with embedded bone cells and surrounding osteoclasts. Fig. 117 shows a more cellular spindle-celled area with many malignant tumour cells.

The patient was readmitted 8 months later with a large local recurrence with satellite cutaneous nodules and cyanosis and dyspnoea. Radiographs of the chest showed broadening of the mediastinum. She died 3 weeks later, 9 months after mastectomy.

Autopsy showed the local recurrence, the mediastinal deposit and others in pleura, pericardium, lower cervical vertebrae, apex of lung and on the endocardial surface of the right ventricle. The histological appearance of the metastases was mainly fibrosarcomatous with occasional multinucleated giant cells (osteoclasts ?) but no osteoid or bone.

Case 40.

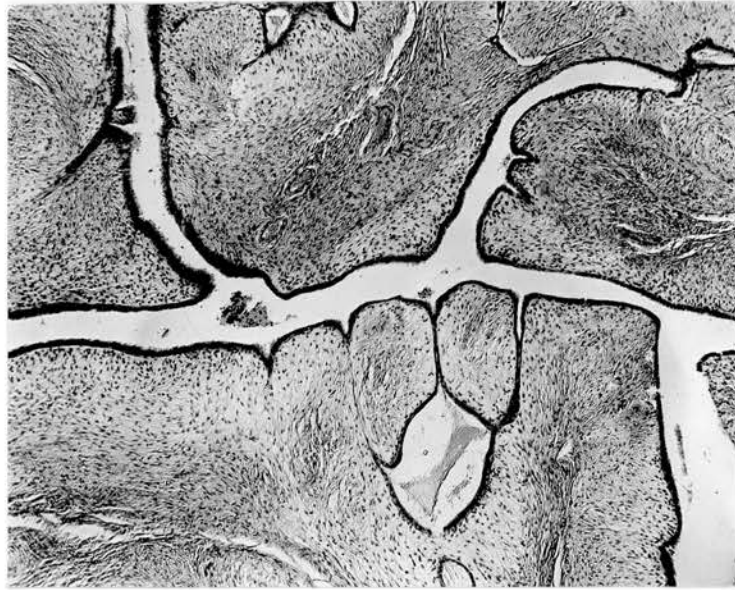


Fig. 114.

x 50.

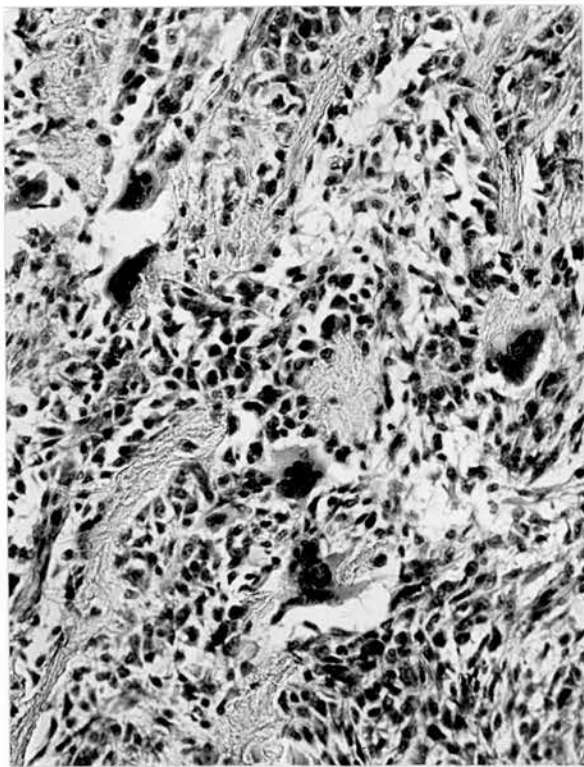


Fig 115.

x 200.



Fig 116.

x 100.

Case 40.

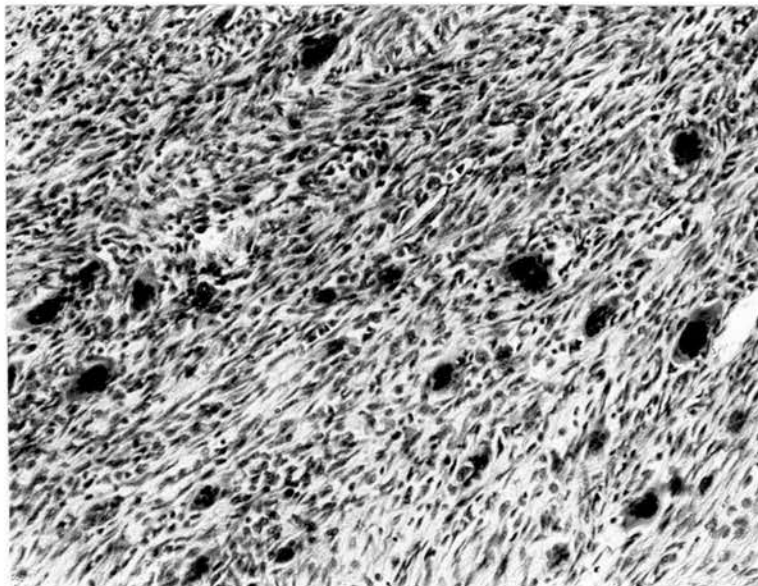


Fig. 117.

x150.

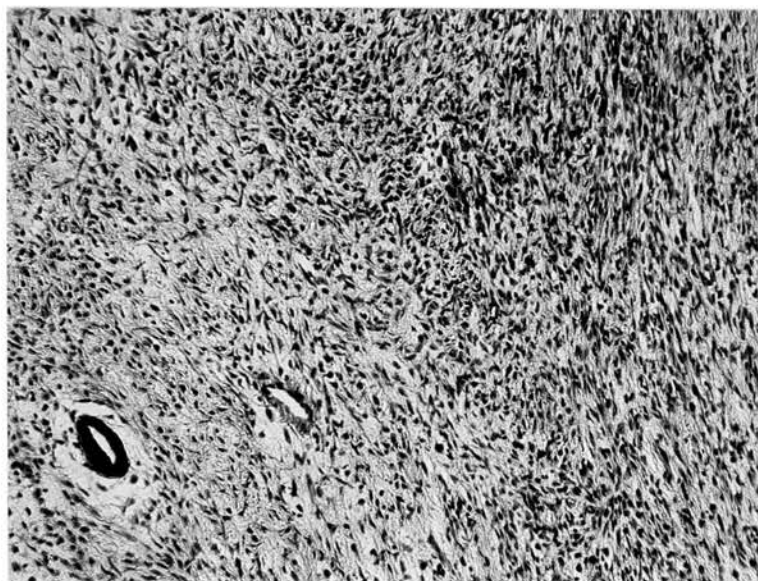


Fig. 118.

x100.

Case 41.

S.167.

History: The patient aged 32 was uncertain when the tumour was first noticed but it was removed when a 7 months lactation stopped.

Examination: About half the tumour is shown as a mounted section (fig. 119). Most of it lies within a well formed capsule but soft cellular masses are also outside it.

Histology: The structure shows much variation in the different areas. Oval masses of malignant pleomorphic cartilage at the tumour periphery (fig. 120) are continuous with a cellular undifferentiated sarcoma. An ill-defined, large cartilaginous area (fig. 121) passes into pleomorphic myxoid growth with perivascular activity and scattered monstrous cells (fig. 122). The masses outside the capsule and invading the fat are fibroblastic in type (fig. 123). The patient was alive and well 8 years after operation.

This is an unusual case, because of the young age, the long survival and the very variable and in areas, the highly malignant histology.

Case 42.

758.

History: The patient aged 70 had a lump in the breast for many years. There was no history of injury.

Examination showed a firm, rounded mass 5 cm. in diameter (a quarter of the transected tumour is shown as a mounted section in fig. 124). It was near the nipple but not adherent to it or to skin. It was defined, with bone in one area.

Histology: Poorly formed bone is shown in a limited area (figs. 125 & 126). The non-ossified tissue has many large irregular cells which suggest tumour cells rather than histiocytes (fig. 128) and patchy deposits of cholesterol crystals (fig. 127). The few multinucleated cells are not osteoclasts. No later note is obtainable on this tumour.

This is a difficult case with very unusual structure. It is apparently a sarcoma, but with no evidence of pre-existing fibroadenoma, though an intra-tumour fibrous strand shows small, benign ducts (fig. 129).

Case 41.

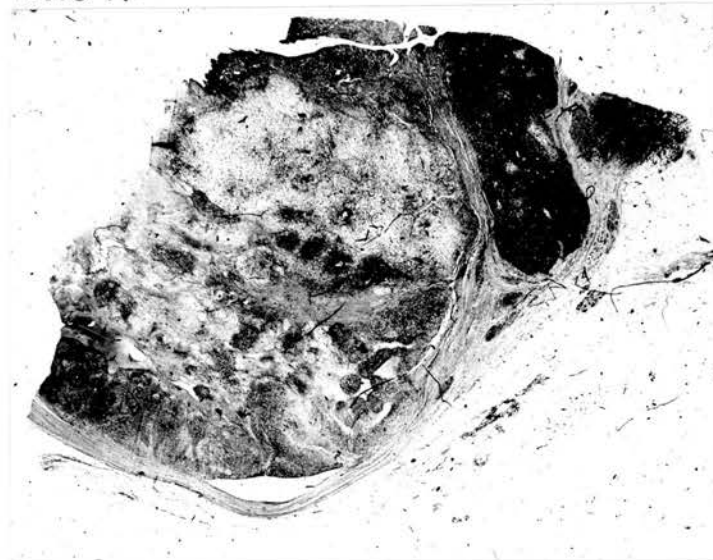


Fig 119.

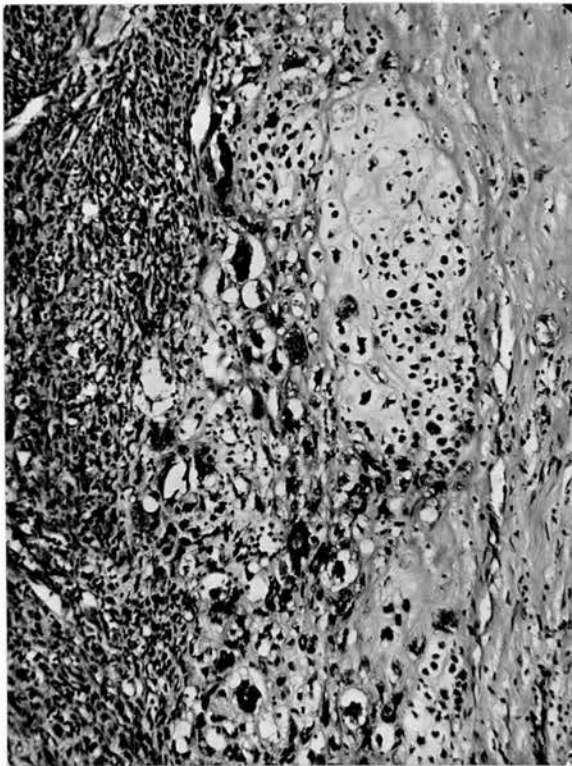


Fig 120.

x 100.



Fig. 121.

x 100.

Case 41.

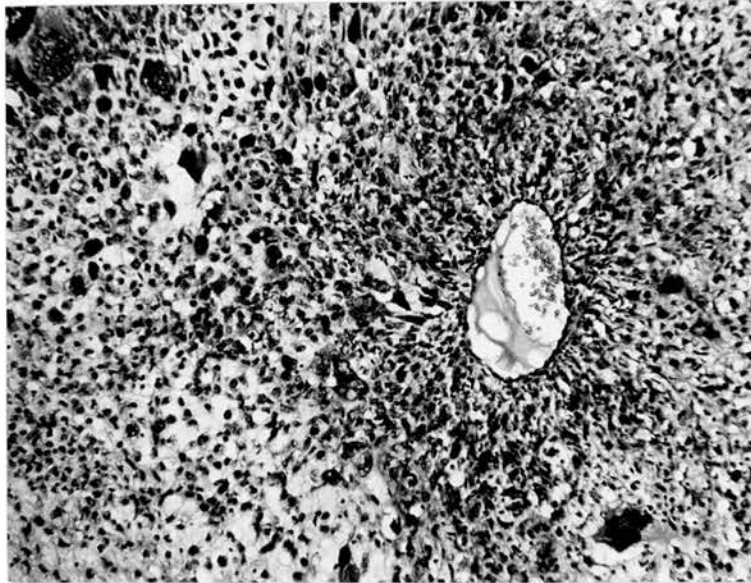


Fig. 122

x 100.

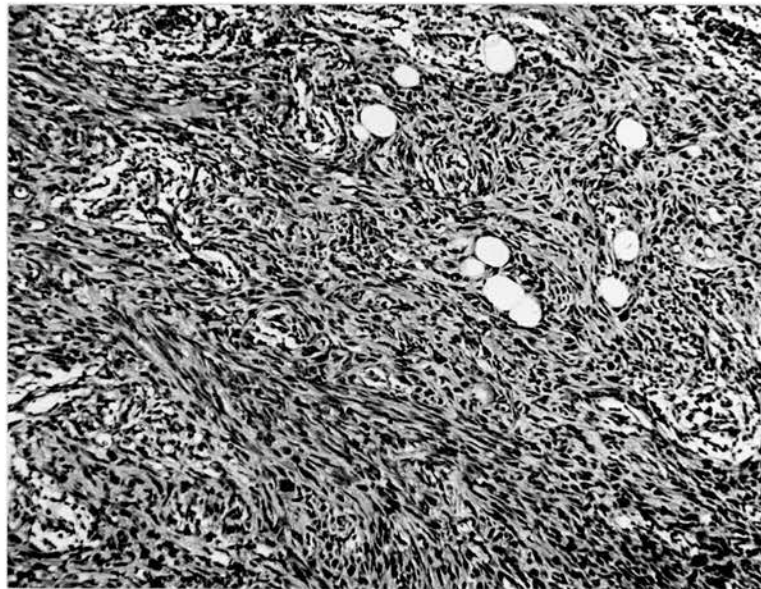


Fig. 123.

x 100.

Case 42.



Fig. 124.

x2.

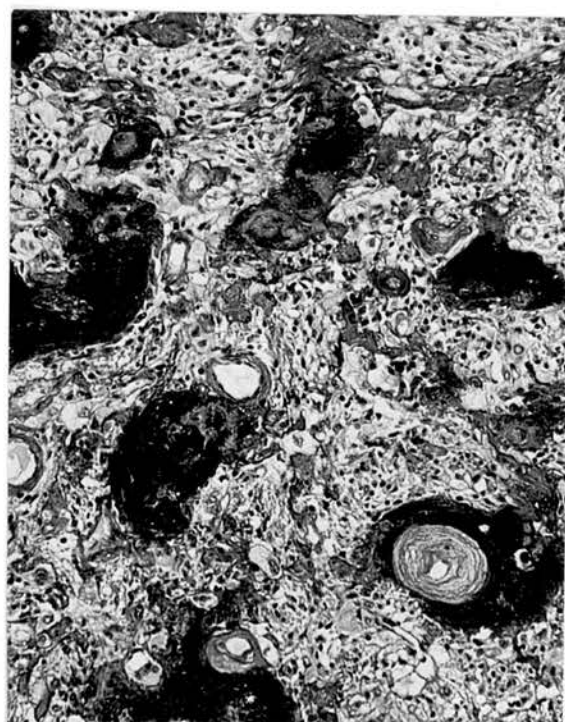


Fig. 125.

x 150.

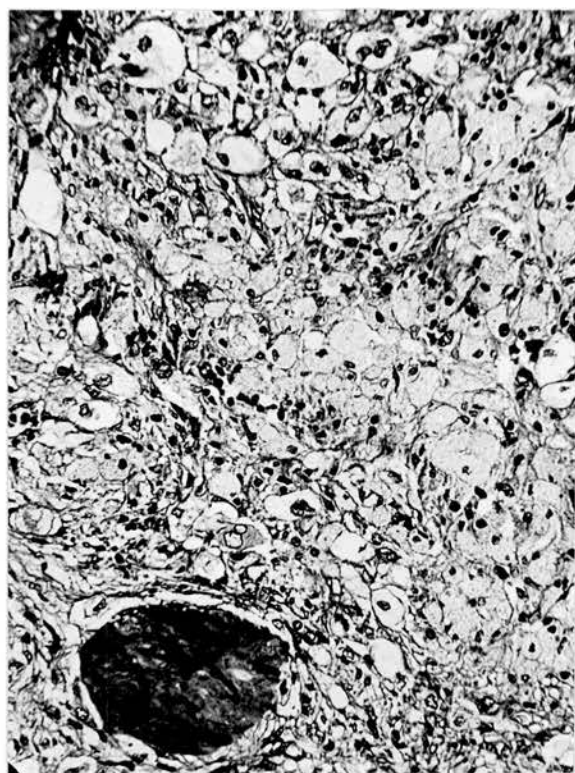


Fig. 126.

x225.



Fig. 127.

x 150.

Case 42.

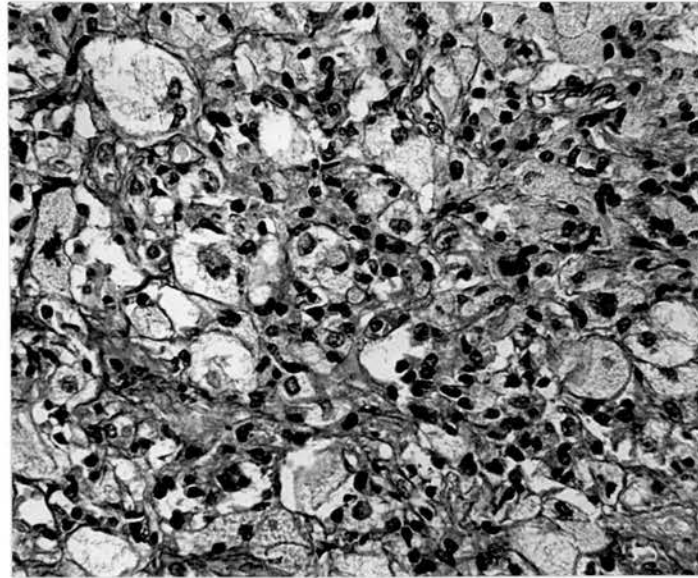


Fig. 128.

× 325.

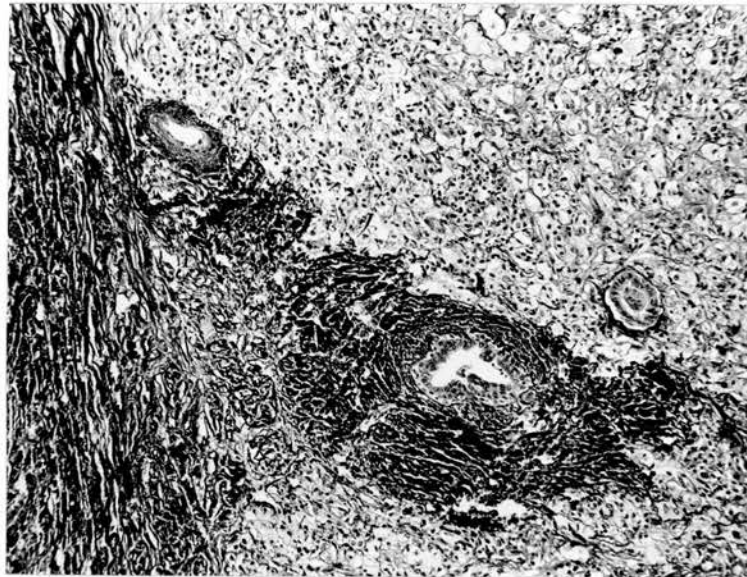


Fig. 129.

× 100.

Case 43.

S.27.

History: The patient aged 59 had known of a tumour in the breast for 18 months. It felt very hard. There was no discharge from the nipple.

Examination: It appeared to be a carcinoma, defined and very hard. A radical mastectomy was done and small nodes were found in the axillary tissue.

Histology: The tumour was cut in two planes. The larger shows a spherical defined tumour of 4 cm. in diameter but suggestive of some early infiltration into fat and muscle (fig. 130). The smaller plane shows an irregular lobulation with a more infiltrative appearance (fig. 131). Much of the tissue has a loosely perivascular structure with cells separated by an intercellular fibrillar matrix. This changes to early non-calcified bone, the diffuse osteoid tissue illustrated in fig. 132. A few glandular elements survive at the periphery. There is no capsule formation. None of the 8 axillary nodes examined showed invasion and the patient was alive and well 18 months later but she died 3 years and 4 months after operation.

Spherical defined tumours such as this one are sometimes mistaken for a rounded defined carcinoma of malignant papillomatous structure and vice versa. A clinically similar tumour to this sarcoma is shown in fig. 133, a carcinoma with a well-defined capsule and its early invasion by the tumour (fig. 134) which also involved the axillary nodes.

Case 44.

S.141.

History: The patient aged 56 had known of the tumour, apparently inactive for 21 years, but enlarging a few weeks before examination.

Examination: A firm tumour was found in the lower quadrant about 8 cm. in diameter, defined and mobile with the overlying skin somewhat atrophic. On transection it was grey and solid but with several small cavities which felt gritty.

Histology: Histogenesis from an intracanalicular fibroadenoma is shown with polypoid masses containing fibroblastic and osteoid tissue with osteoclasts (fig. 135).

Cavities with fresh blood are surrounded by osteoid tissue, osteoblasts and osteoclasts (fig. 136) with some undifferentiated stroma. This picture is similar to other cases illustrated in this series. Bone formation at various stages is seen in figs. 137, 138 & 139 with many mitotic figures. The patient died but the exact date is not known.

Case 45.

1137.

Few data are available for this case but the tumour had been reported elsewhere as a mucinoid ("colloid") carcinoma of the breast.

Examination showed a large lobulated gelatinous-looking mass (fig. 140).

Histology shows early cartilaginous metaplasia in a mildly pleomorphic fibroblastic matrix (fig. 141). At a deeper level there are more defined cartilaginous foci and pectoral muscle invasion by less differentiated tumour (fig. 142).

Case 46.

1402.

Whole breast sections in two planes with axillary lymph nodes were sent without data. The tumour is defined in both planes; the nodes are largely replaced by fat (figs. 143, 144 & 145).

Histology: The generalized lobulated structure indicates histogenesis in an intracanalicular fibroadenoma growth (fig. 146). The stromal polyps defined against less cellular fibrous tissue show small foci of partly calcified osteoid formation (figs. 146 & 147). Most of the epithelium covering the polyps has disappeared but small ducts are found outside the polyps (fig. 147). An unexpected finding was an irregular mass of squamous carcinoma (fig. 149).

Case 43.

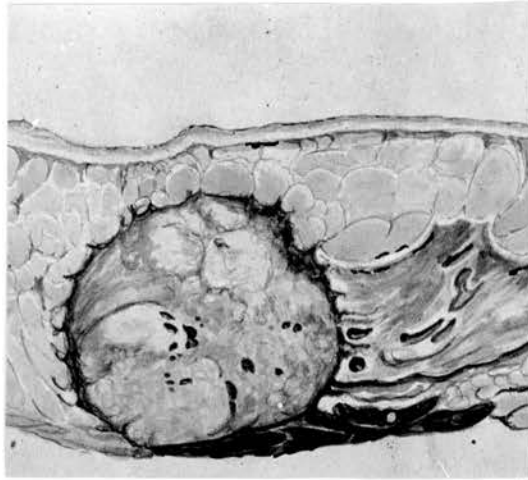


Fig. 130.

x 1.

Fig. 131 in other volume only.



Fig. 132.

x 250.

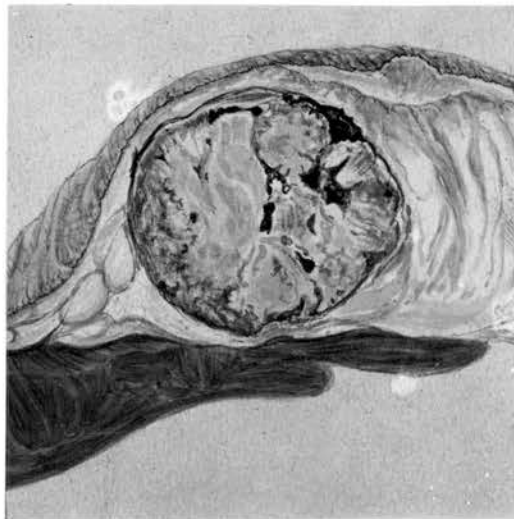


Fig. 133.

x 1.

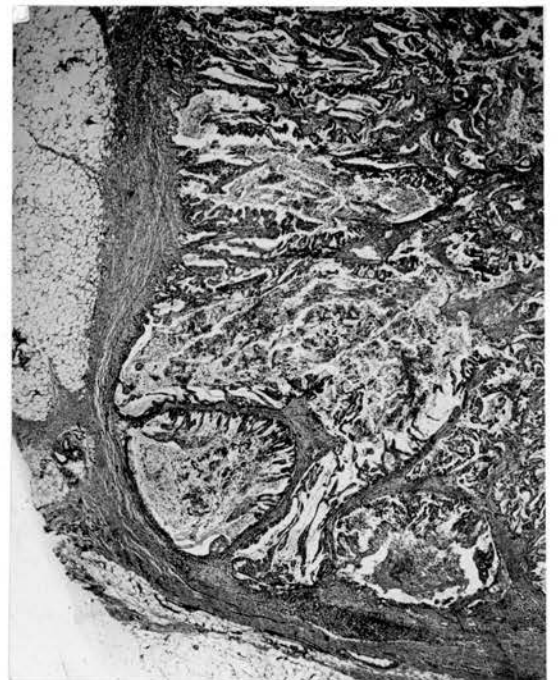


Fig. 134.

x 50.

Case 44.

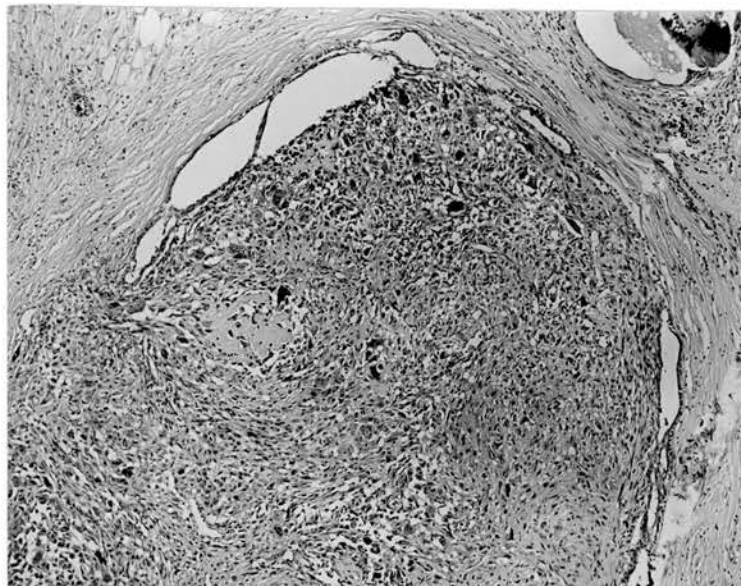


Fig. 135.

×55.

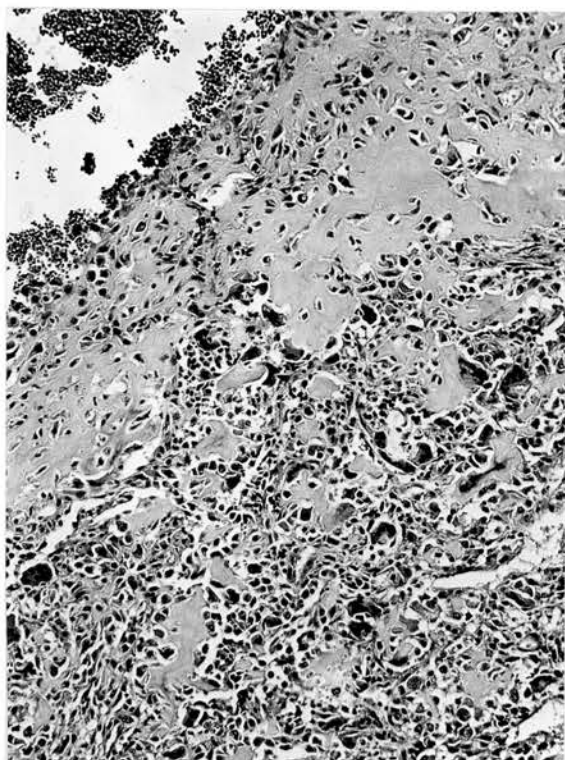


Fig. 136

×100.

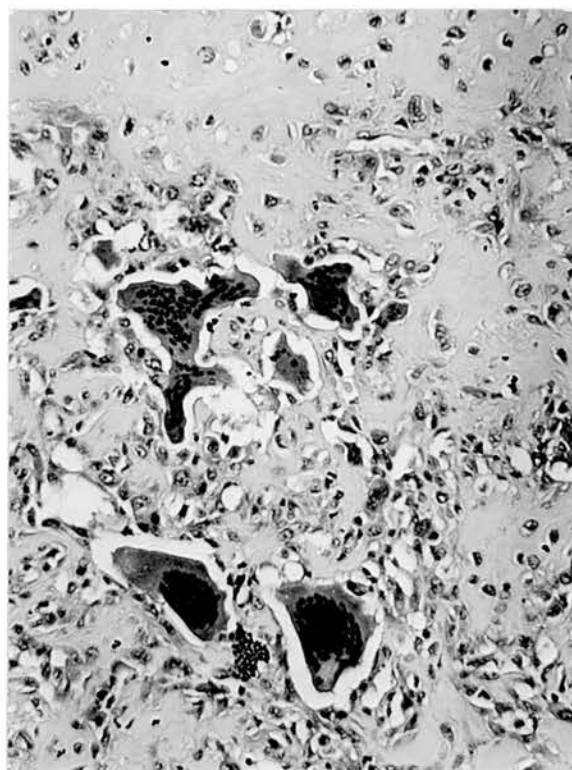


Fig. 137.

×150.

Case 44.

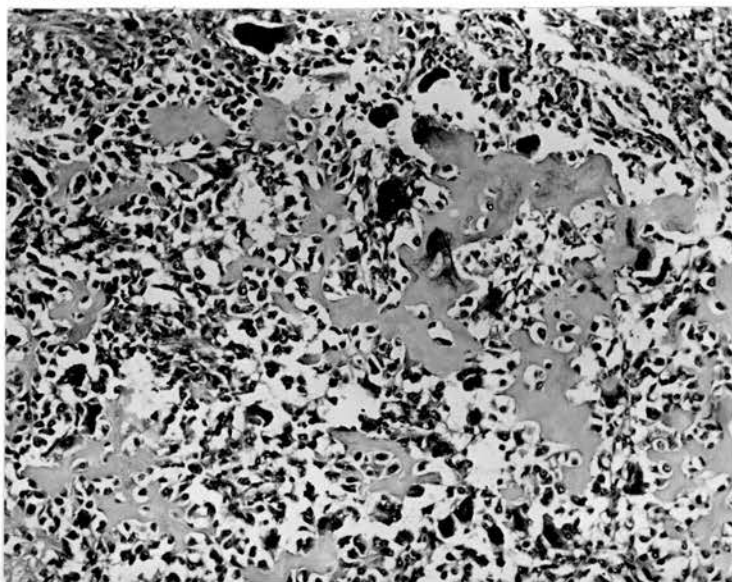


Fig. 138

× 150.

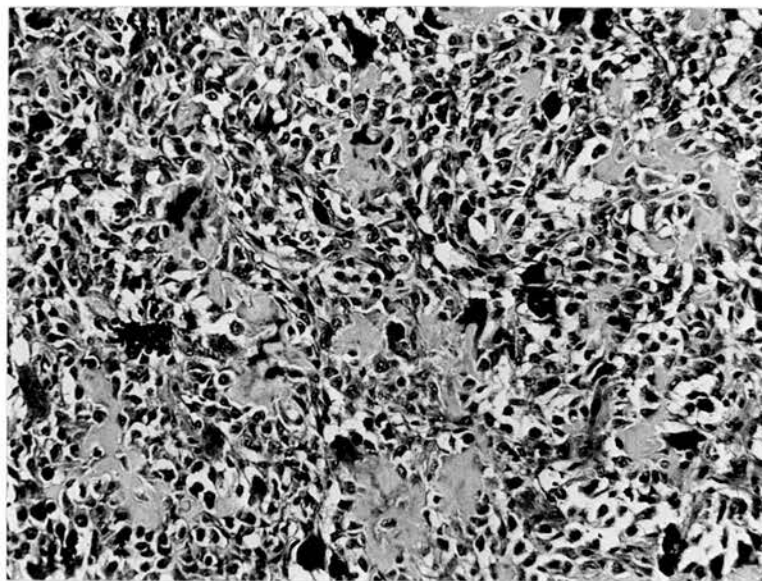


Fig. 139.

× 120.

Case 45.

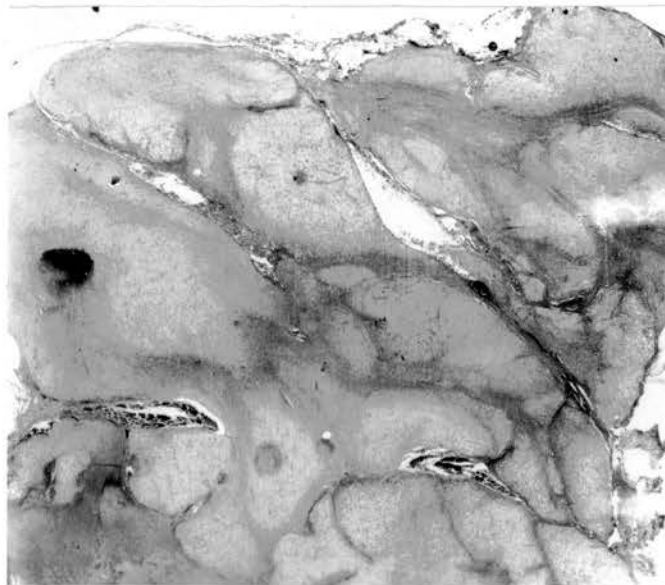


Fig. 140.

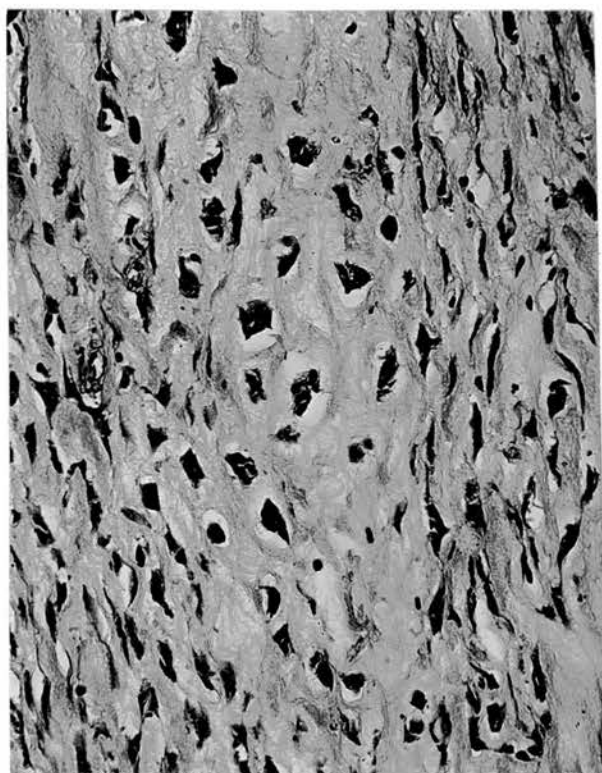


Fig. 141.

x250.

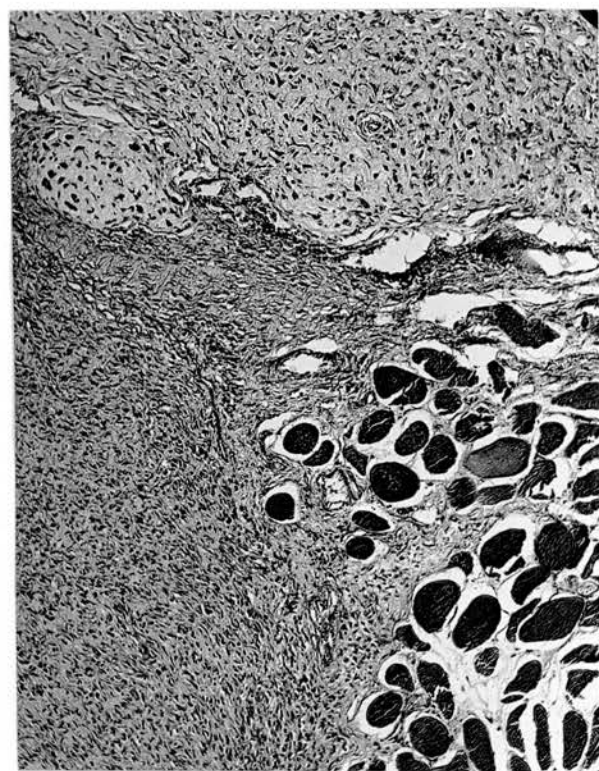


Fig. 142.

x70.

Case 46.

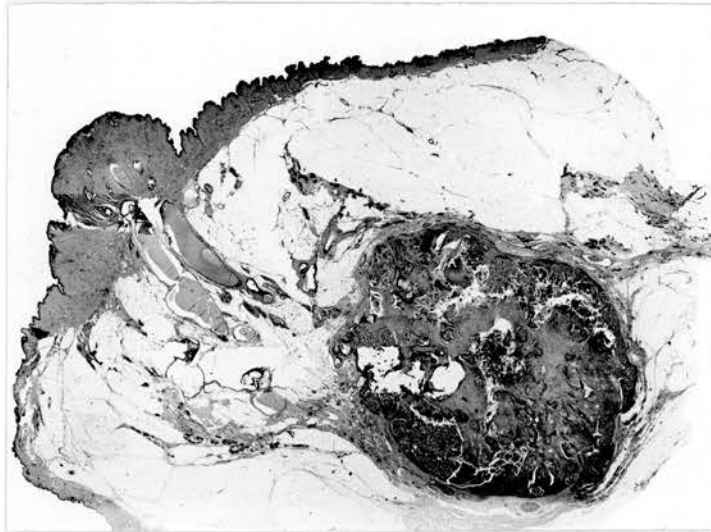


Fig. 143.

x1.

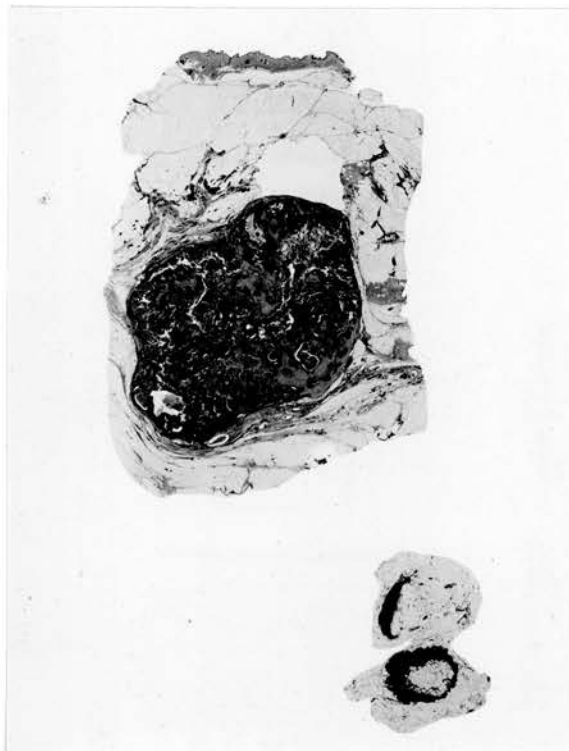


Fig. 144.

x1.

Fig. 145.

Case 46

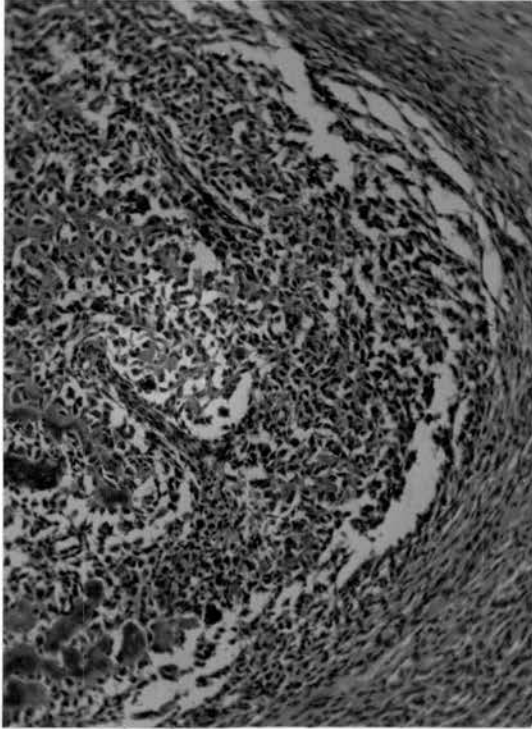


Fig. 146

×100

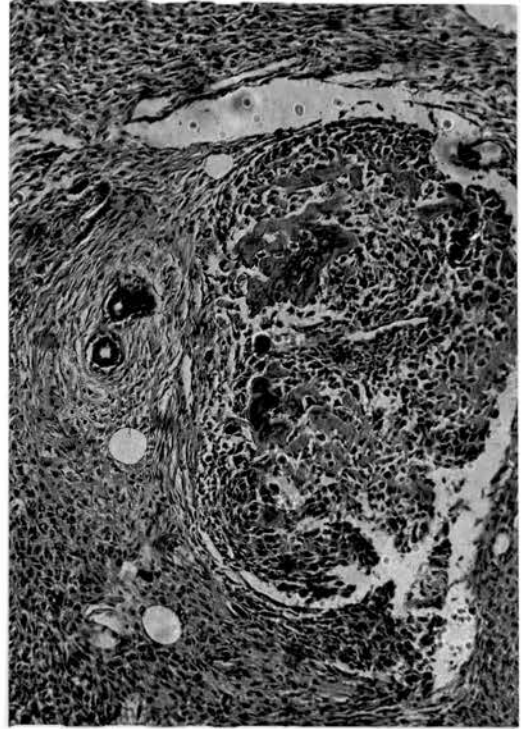


Fig. 147.

×100.

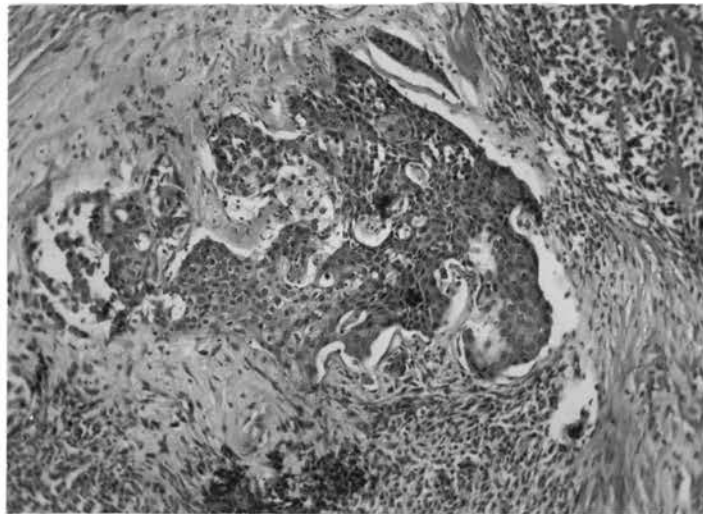


Fig. 148

×100.

Case 47.

S.147.

History: The patient aged 57 years, knew of the tumour in the breast for 2 months.

Examination: It appeared to be a cystic "Brodie's Tumour" but when incised it was obviously malignant, a fungating tumour with much haemorrhage and sloughing. Radical operation was followed by palliative irradiation.

Histology shows an active fibroblastic tissue in which are areas of malignant cartilage (fig. 149). An included duct shows hyperplastic, desquamating epithelium which suggested carcinoma. There were no clinical metastasis. She died 1 year 10 months after operation.

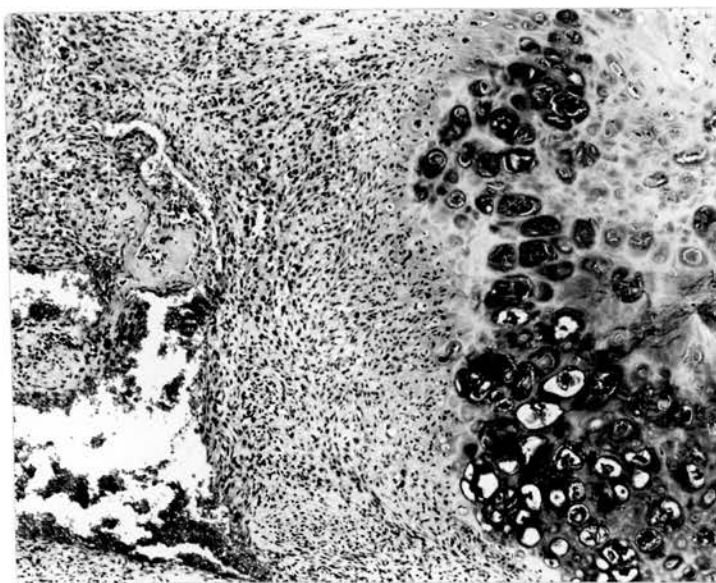


Fig. 149.

x70.

Case 48.

S.17.

History: The patient aged 56 years, said the tumour appeared after a blow on the breast, 2 years previous to examination. There was a recent nipple discharge of 2 weeks duration.

Examination suggested a haematoma, with ulceration and recent blood clot over much of the mammary area. No palpable axillary nodes.

Histology: A highly malignant sarcoma with haemorrhage, necrosis and numerous mitotic figures in the intact tissue. No mammary gland tissue was found. Some areas show pleomorphic cells proliferating round blood vessels (fig. 150). There are scattered foci of early cartilage formation (fig. 151) confirmed by mucin staining, but much of the malignant tissue is active fibrosarcoma (fig. 152).

Case 49.

S.165.

History: The patient aged 59 years had noticed a lump in one breast for 6 weeks.

Examination: A very large fatty breast with a hard irregular lump was excised by radical mastectomy. Transection showed a tumour 5 cm. in diameter with a hard, irregular surface and central calcification.

Histology: A fibrosarcoma with large pleomorphic spindle-cells with moderate mitotic activity. No glandular elements were found in the sections examined. Some areas showed bone formation with osteoblasts and osteoclasts; other parts were necrotic with calcification. The four axillary nodes examined showed no tumour. The patient died 1 year 10 months after operation and there was no autopsy.

Case 48.

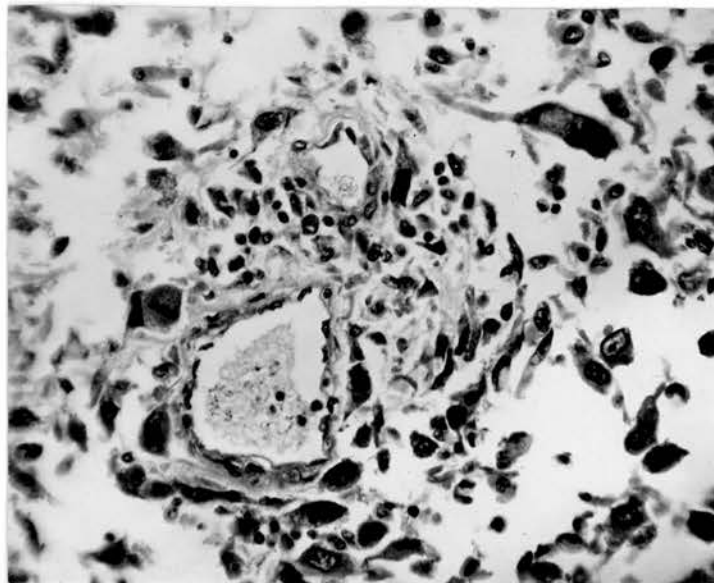


Fig. 150.

x 300.

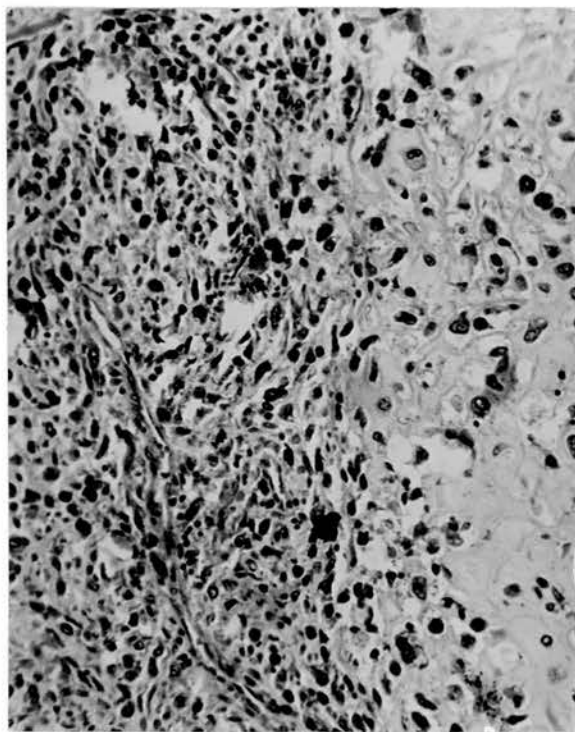


Fig. 151.

x 120.

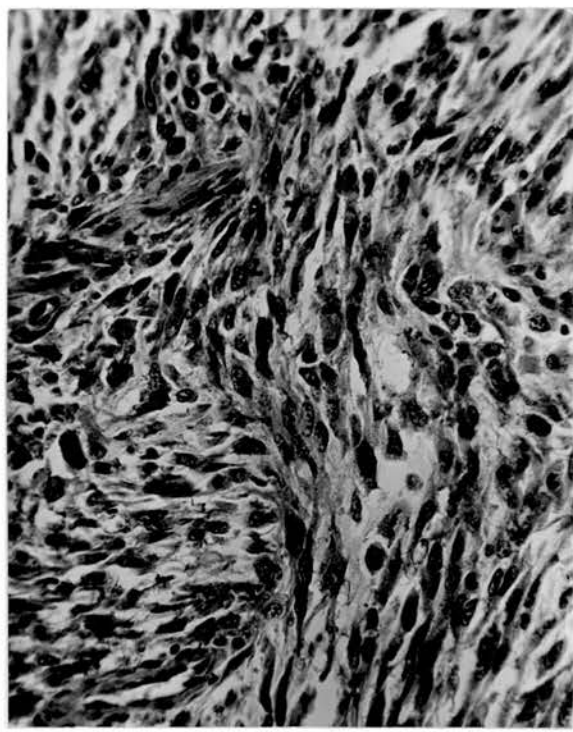


Fig. 152.

x 250.

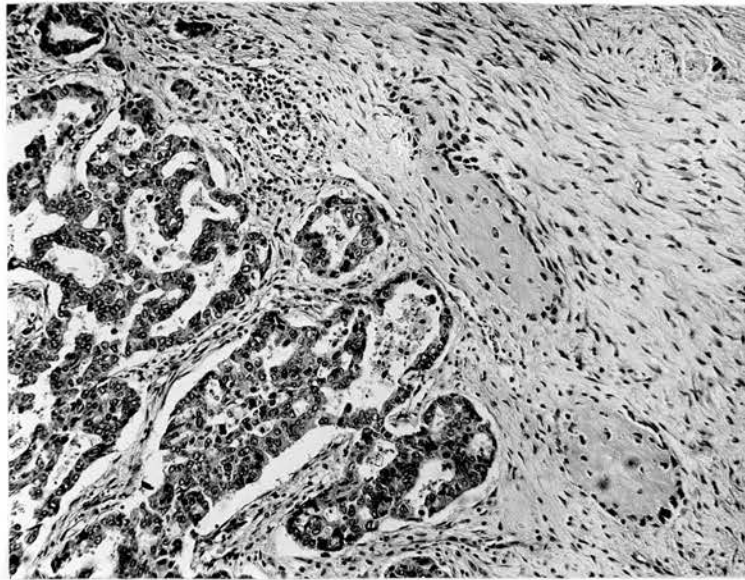


Fig. 153.

× 100.

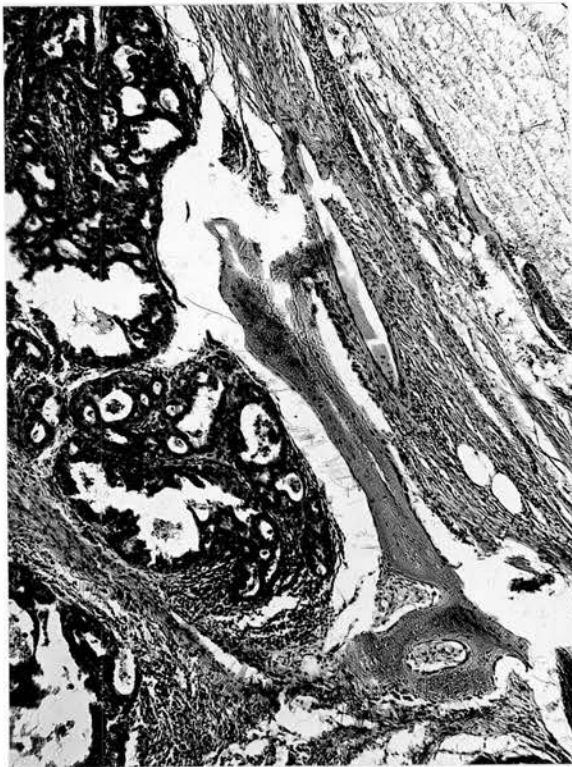


Fig. 154.

× 50



Fig. 155.

× 75.



Fig. 156

x45.

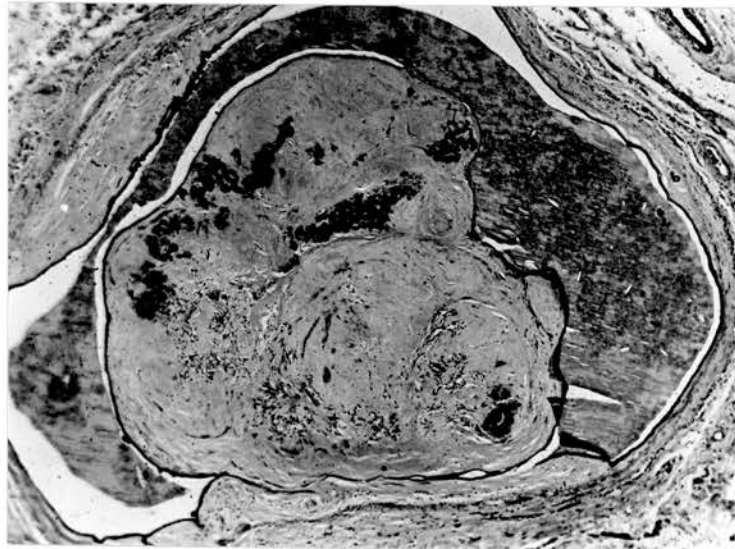


Fig. 157.

x45.

LIPOSARCOMA

Cases 52 - 59. Figs. 158 - 188.

Liposarcoma

In older patients many breasts show extensive replacement of stroma of the corpus mammae by fat of the usual inert type, but lipomatous tumours, benign or malignant are a rare finding.

The liposarcomas are perhaps the most easily recognisable of the mammary sarcomas because of their macroscopic and histological appearances. Transection shows the greyish-yellow colour characteristic of fatty tissue tumours, sometimes with areas of mucoid appearance indicative of lipomyxomatous structure. The tumours may be large and lobulated, as in other sites and in the first example shown here. There is characteristically considerable variety of histological structure ranging from sheets of small nondescript cells to a very pleomorphic picture of large lipoblasts with highly atypical nuclei and granular or vacuolated cytoplasm which gives a fat-positive reaction. Sarcomas of other types may also show a highly pleomorphic cytology and a fat stain is usually necessary to confirm a diagnosis of liposarcoma, but the characteristic picture of many lipoblastic tumours especially when exhibiting mucoid areas need not always demand the demonstration of fatty metaplasia.

Liposarcomas in general are often described as "malignant from the beginning", but Stout (1944) and Pack et al (1954) have found transitions from benign to malignant fatty tumours and I have examined similar transformations, at all stages. Malignant fat may also be found in some fibroblastic sarcomas with transitions from fibrosarcoma to fibrolipoma to extensive liposarcoma in the recurrent tissue giving the appearance at operation of a purely lipomatous malignancy.

A case of special interest is described later (Case 52). This is an example of carcinosarcoma in which the stromal element was liposarcomatous. Recurrences appear histologically less malignant i.e. they may show a cellular lipoma picture without abnormal cells or may be largely myxomatous, a type which has been already emphasised here as a primitive tissue with ominous outlook.

Liposarcoma

| Series | Reference | Age | Duration of tumour (years). | Type | Nodes | Therapy | Outcome in years. | Metastases |
|--------|-----------|-----|-----------------------------------|------------------|-------|---------------------|--------------------------|---------------------------------|
| 52 | S. 112. | 82 | 1/12 | Liposarcoma. | - | Simple mastectomy | Died 3 ⁹ /12 | ? |
| 53 | 1399 | 44 | Several yrs. | do. | - | Initial irradiation | ? | - |
| 54 | S. 107 | 38 | 25+ Recent growth 2 yrs. | do. | - | Local excision | Alive 2 ⁷ /12 | - |
| 55 | S. 14 | 37 | ? | do. | - | Local excision | Recurrence Died 4/12. | ? |
| 56 | S. 95 | 23 | ? | do. | - | ? | ? | - |
| 57 | 1401 | 64 | ? | Myxoliposarcoma | - | ? | Local Recurrence | - |
| 58 | S. 146 | 56 | 6/12 | Fibroliposarcoma | - | Local excision | Died | Lungs + Before operation. |

For Comparison

| | | | | | | | | |
|----|------|----|---|------------------------------|---|------------------------------------------------|---------------------------|------------------------|
| 59 | 23.4 | 44 | ? | Myxoliposarcoma in thigh. | - | Local excision and hind quarter amputation. | 2 Recurrences Died 10. | Pelvis and abdomen. |
|----|------|----|---|------------------------------|---|------------------------------------------------|---------------------------|------------------------|

8 examples of liposarcoma are illustrated in this mammary study.

Case 52.

S.112.

History: A married woman aged 82 years had noticed a mammary swelling for 1 month.

Examination showed a large defined fairly movable mass in a fatty breast. It was removed by simple mastectomy as the clinical diagnosis was uncertain but no nodes were palpable. Transection showed a fatty breast in which below the nipple was a large oval tumour, greyish-yellow in colour and 7.5 cm. in its transverse diameter, with areas of haemorrhage and necrosis (fig. 158). The periphery, though generally well defined and somewhat lobulated, showed some early infiltration of the surrounding fat. Little mammary tissue could be identified in or near the tumour except on the upper aspect where several of the main ducts leading to the nipple were prominent because of their thickened walls. Some of these ducts suggested infiltrative growth into the underlying tumour tissue.

Histology: Six areas of the tumour and 2 of the thickened ducts above it with some underlying tissue were examined. All tumour areas showed a malignant growth of very varied structure. Some areas were highly pleomorphic with monstrous multinucleated cells with a vacuolated cytoplasm strongly positive for fat (fig. 161). Mitotic figures were found mainly in the smaller cells which formed a matrix to these large bizarre elements. Other areas showed a few scattered monstrous cells with fat vacuoles of varying size in cellular sheets of small, mainly round and polygonal cells (fig. 160). Other areas were fibroblastic in structure, with strands of small spindle cells among which were very small fat cells (fig. 159). Blood vessels were not very prominent in the sections examined but mitotic figures were easily recognised in all areas.

A few small normal ducts were present near the lower periphery (fig. 159) but the thickened main ducts above the upper margin of the tumour showed intraductal carcinoma, of "comedo type" with associated infiltrative downgrowth into well-differentiated adjacent tumour tissue (fig. 162) and deeper penetration into more typical liposarcomatous growth (fig. 163.) There was no transition between the carcinomatous and sarcomatous components.

The picture in figs. 162 & 163 indicates an accidental merging of two separate and distinct malignant tissues and might be described as the "collision" type of carcinosarcoma.

The patient was alive 3 years after operation but with a large ulcer in the axillary skin and her general condition was rapidly deteriorating. She died at home 3 years 9 months after mastectomy. There was no autopsy.

This was an advanced sarcomatous condition when first examined and shows several aspects of a typical liposarcoma. Little if any indication of the possible transformation of benign to malignant lipomatous growth could be found in the 8 areas examined.

Case 53.

1399.

History: The patient aged 44 had noticed a lump in the breast for several years. It was diagnosed clinically as chronic mastitis and treated by short wave therapy but continued to increase in size. Five years later she returned for further investigation.

Examination: The tumour was now large, measuring 10 x 6 x 6 cm., fairly homogeneous, yellowish-grey and myxomatous looking. The pathologist considered it sarcomatous and additional sections stained with Sudam III confirmed its lipomatous nature.

Histology of the small biopsy tissue available shows ducts adjacent to mature fat cells in a mucinous background (fig. 164). Other areas are mainly of myxoid appearance with scattered large lipoblasts showing vacuolation of both cytoplasm and some of the nuclei (figs. 165, 166 & 167). A few mature fat cells are present in all areas.

The characteristic lobulated structure of lipomatous growths is seen in some of the following examples and is also well demonstrated in foetal and post-natal normal fat tissue in areas where in later life fat tends to accumulate. Figs. 168 & 169 show this lobulation in subcutaneous mammary fat in an infant aged 4 months, for comparison with fatty tumours in general.

Case 52.

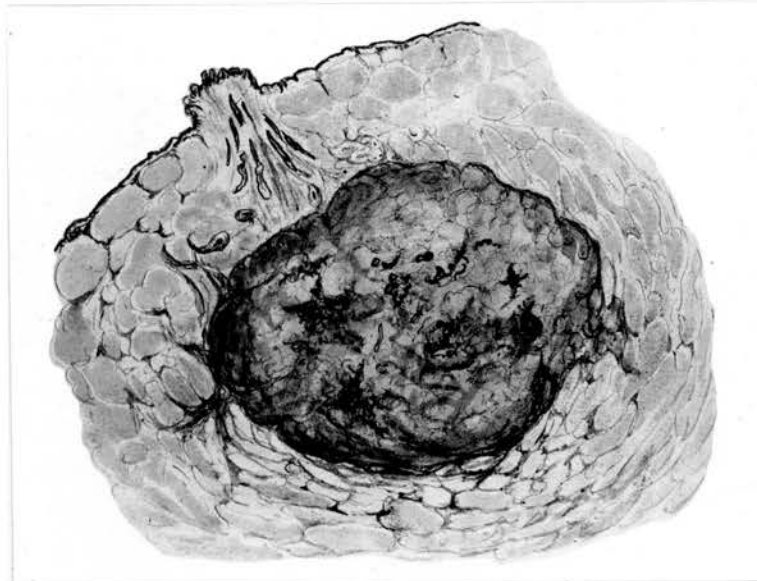


Fig. 158.

x 2/3.

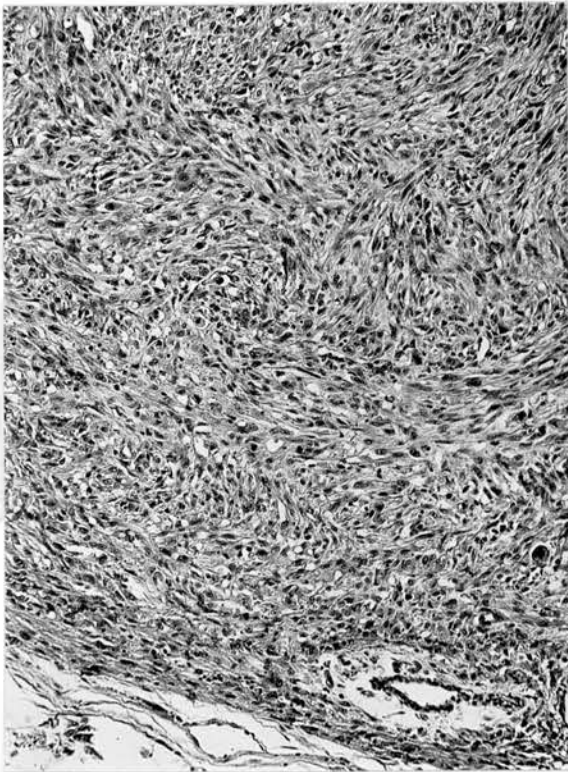


Fig. 159.

x 100.

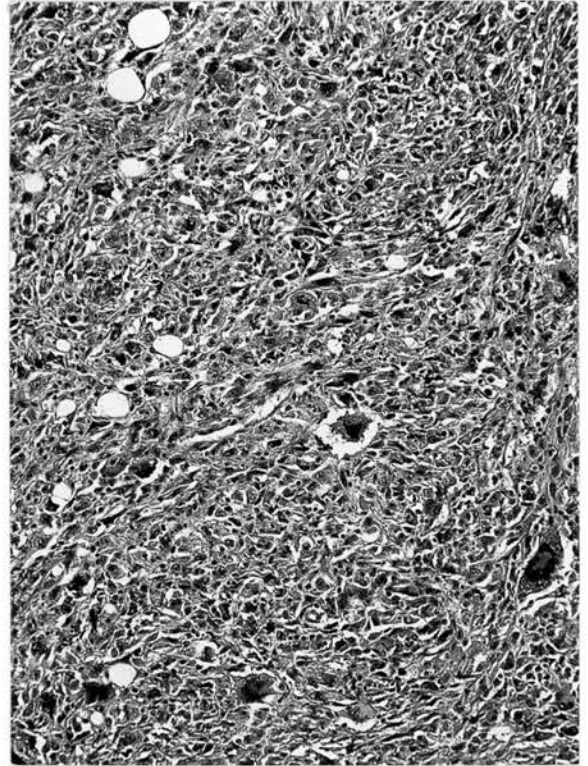


Fig. 160.

x 100.

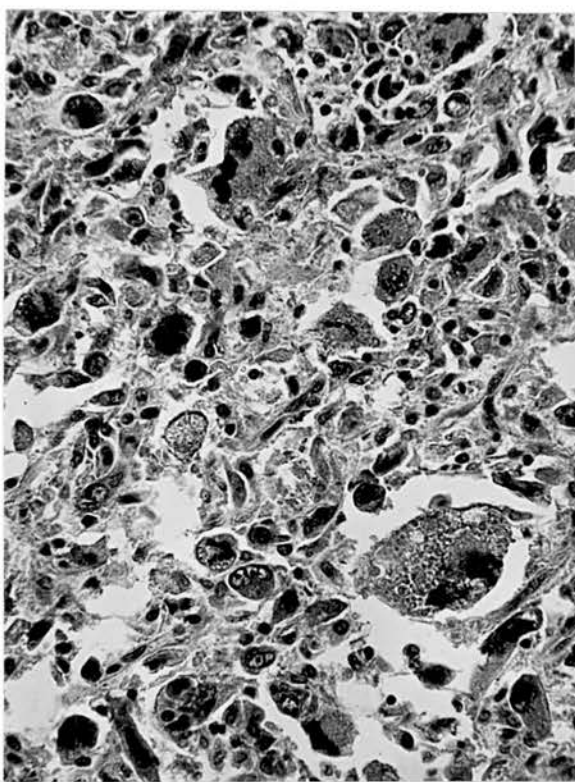


Fig. 161.

x 300.

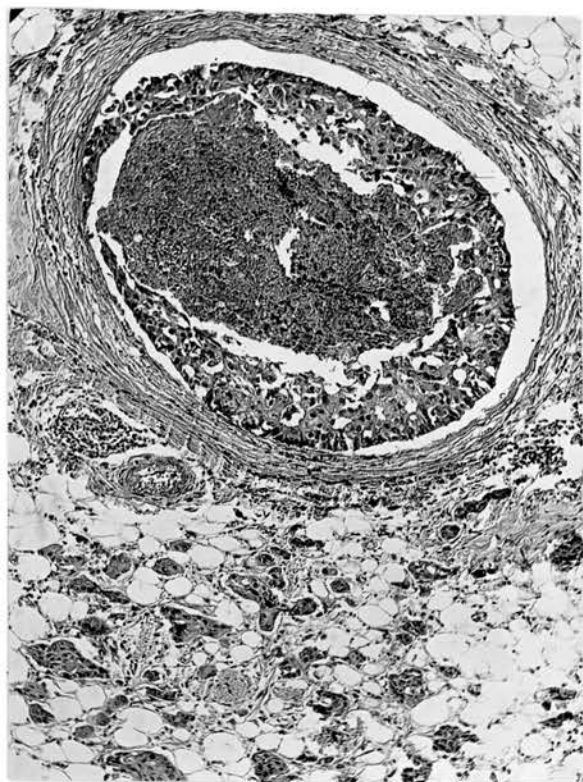


Fig. 162.

x 75.

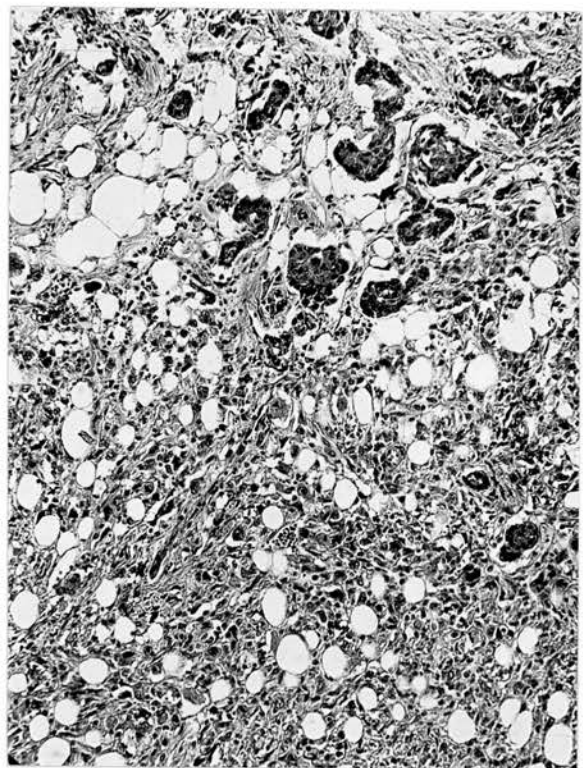


Fig. 163.

x 100.

Case 53.

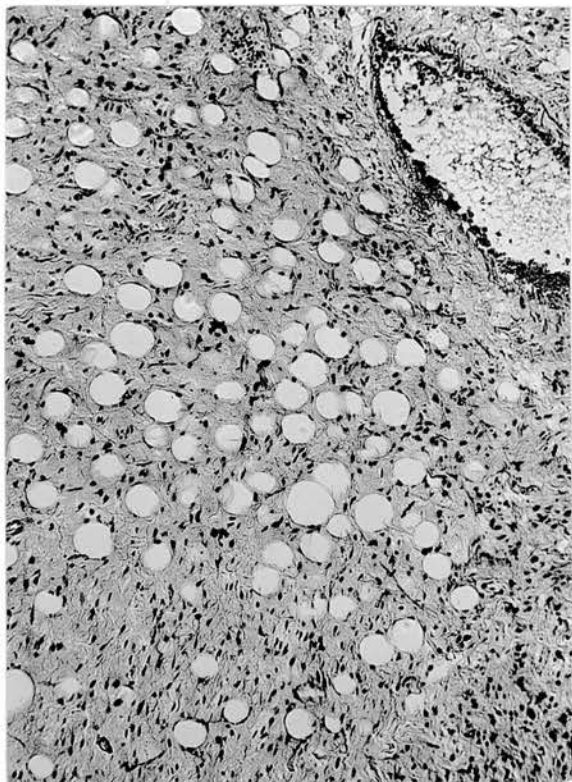


Fig. 164.

x75.

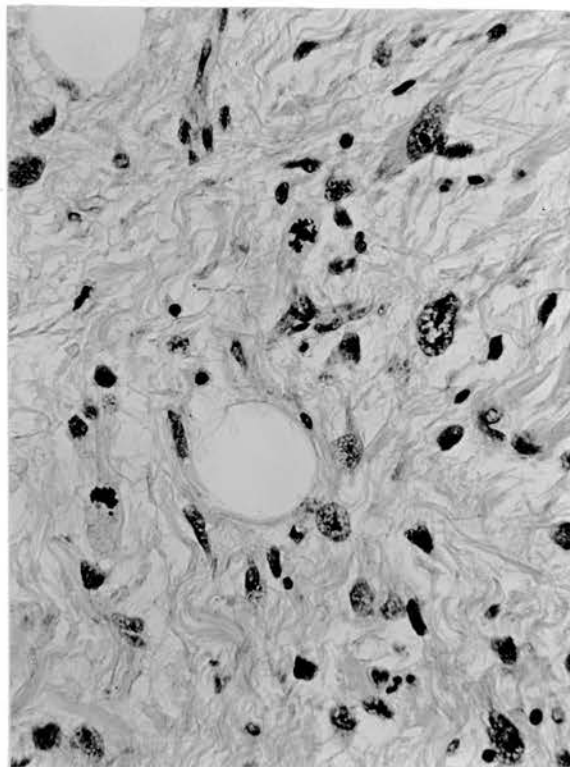


Fig. 165.

x400.

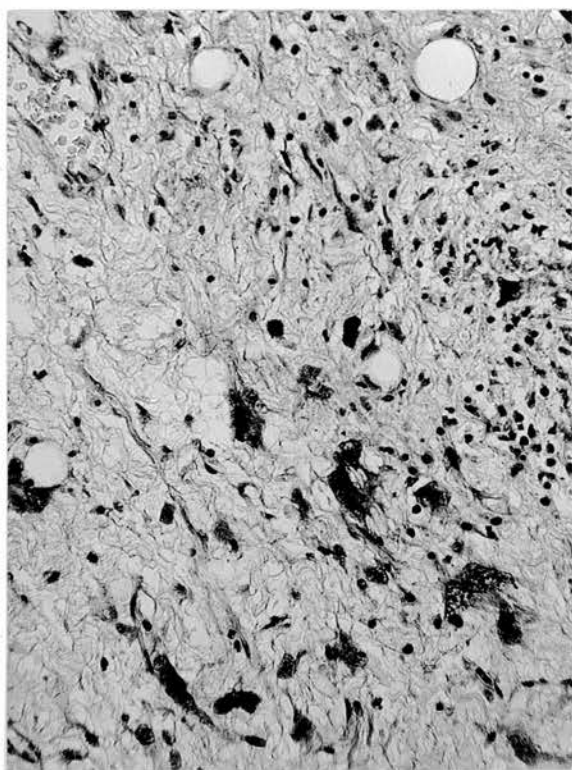


Fig. 166

x225

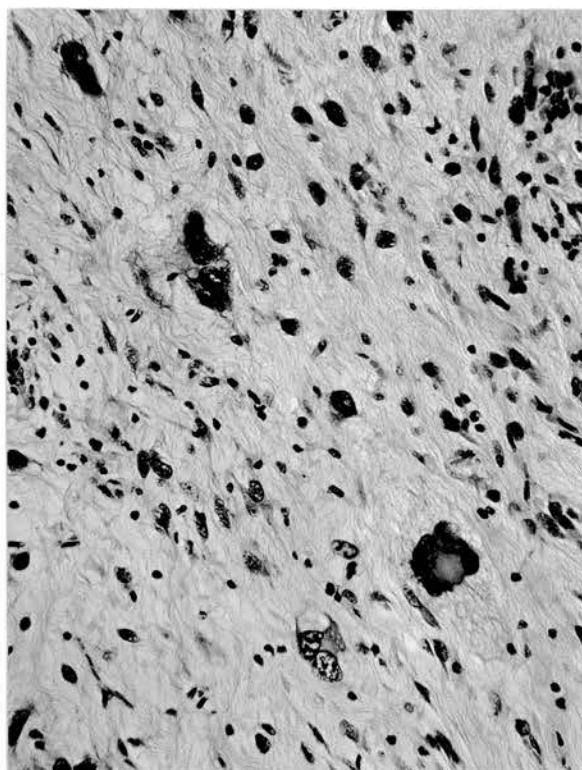


Fig. 167.

x225.

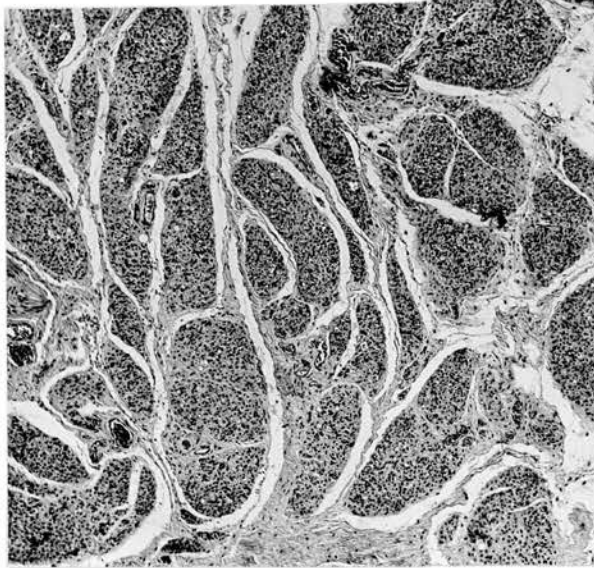


Fig. 168.

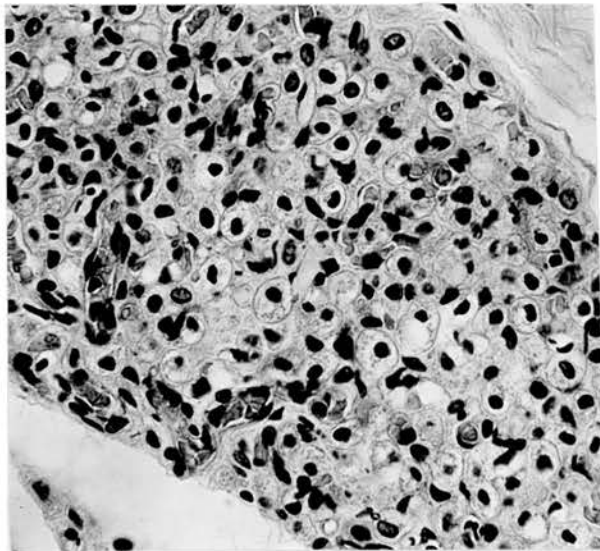


Fig. 169.

Case 54.

S.107.

History: The patient aged 38 years was aware of a lump in the breast since "childhood" (puberty ?). It had increased in size during the 2 years before examination.

Examination suggested a cyst, which was excised with the escape of straw-coloured fluid. Transection showed an irregular cavity 7.5 cm. in diameter largely filled by an irregular, polypoidal mass of solid tissue, suspiciously malignant.

Histology: The tumour has developed from an intracanalicular fibroadenoma and the structure of the benign growth is still evident. The stromal masses of "cauliflower" growth had projected into a cyst formed by a dilated duct (fig. 170). The epithelial covering of these projections is largely desquamated (fig. 171). The sarcomatous tissue which has developed in them is progressively malignant with an early liposarcomatous picture (figs. 172 & 173), becoming in areas the highly malignant pleomorphic structure with vacuolated monstrous cells and atypical mitotic figures characteristic of many obvious liposarcomas (fig. 174). At the periphery of the tumour, small ducts are embedded in sheets of nondescript, rounded and polygonal cells (fig. 175); other areas are completely spindle-celled (fig. 176). The patient was alive and well 2 years 9 months after operation and irradiation.

The sequence of tissue variations here is difficult to trace but figs. 175 & 176 of peripheral areas losing their basic fibroadenomatous lobulation, may be the final, completely undifferentiated stage. It might be argued on the other hand that the line of differentiation was in the other direction i.e. from spindle-cell (fibroblastic) tissue to the large pleomorphic fatty structure.

Case 54.

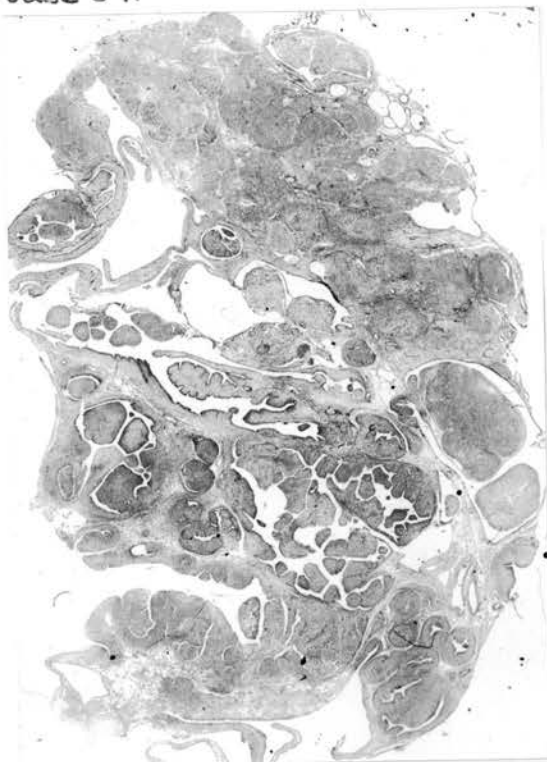


Fig. 170.

x 2.5.

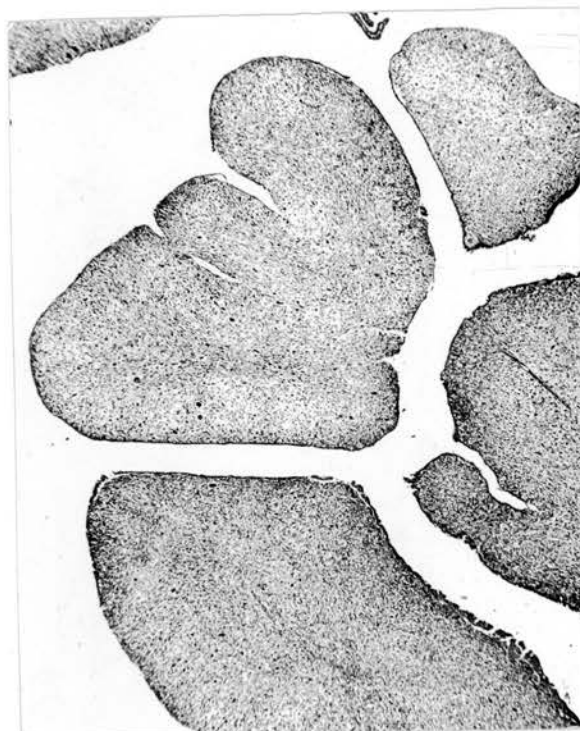


Fig. 171.

x 25.



Fig. 172.

x 100.

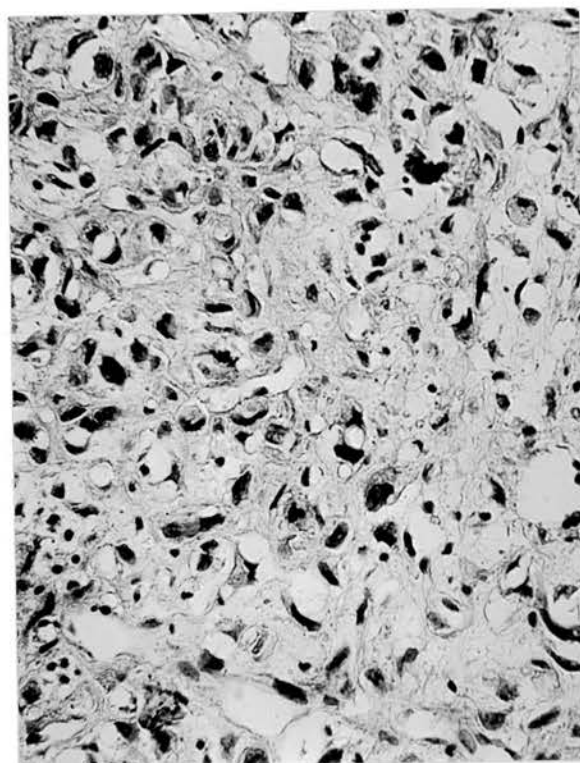


Fig. 173.

x 300.

Case 54.

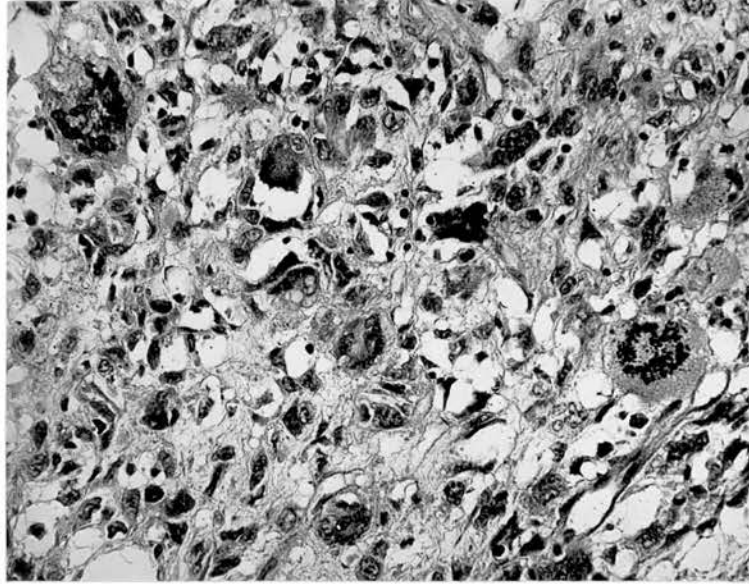


Fig. 174.

x 250

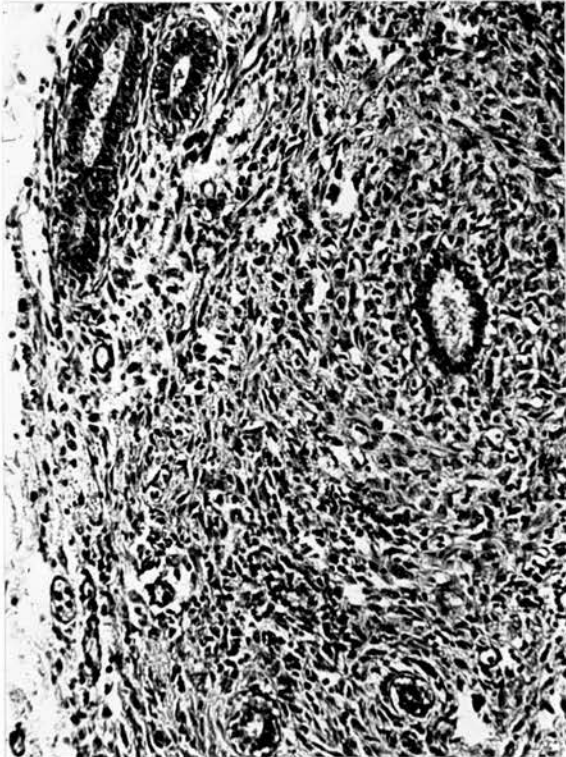


Fig. 175

x 150

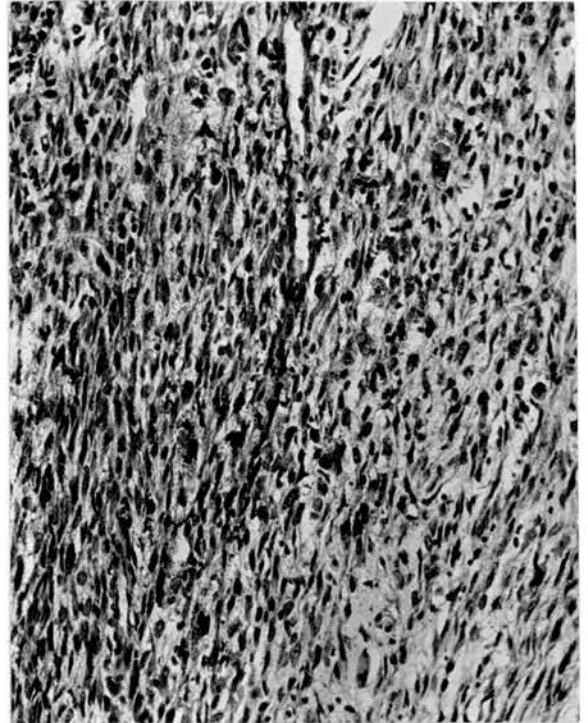


Fig. 176

x 150

Case 54.

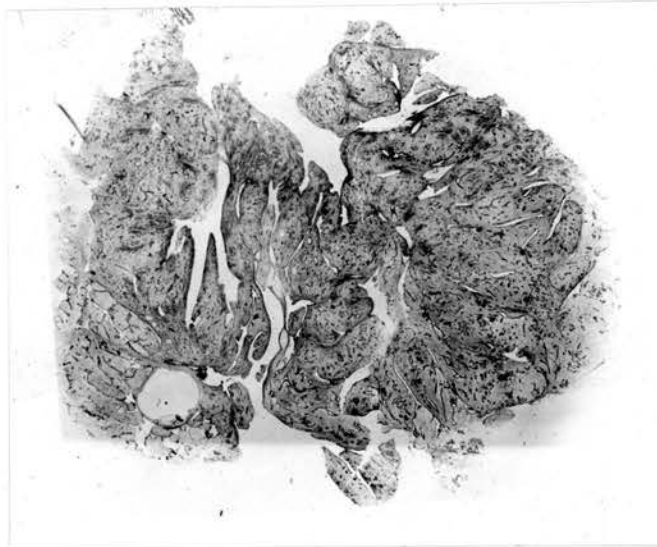


Fig. 177.

$\times 3/4$.

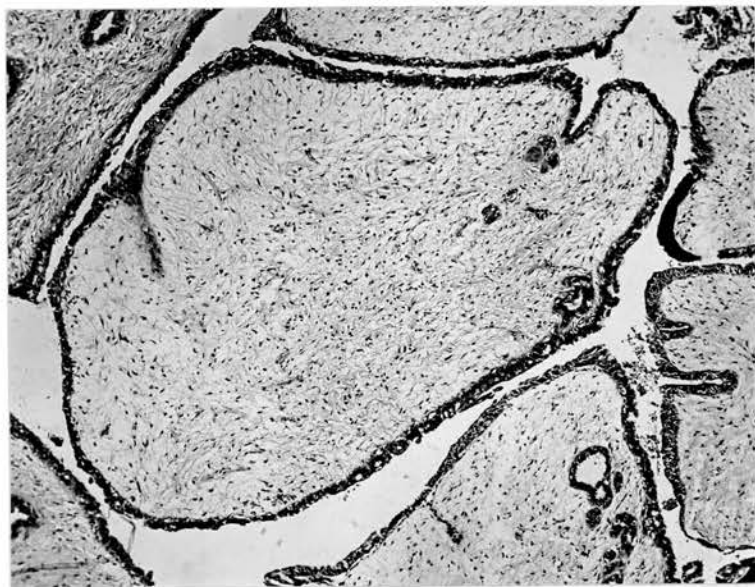


Fig. 178

$\times 50$

Case 55.

S.14.

History: The patient aged 37 was uncertain when the tumour was first noticed.

Examination: The tumour was apparently considered benign as a local excision was done. It recurred rapidly in the operation area as 2 large fungating haemorrhagic tumours, 7 & 10 cm. in diameter. She was then referred for irradiation but the condition was regarded as "too advanced even for reasonable palliation by radiotherapy". She died 2 months later, 4 months after operation.

Histology: The tissue received showed a great variety of structure (a) a plump spindle- and round-cell fairly isomorphic fibrosarcoma with scattered bizarre nuclei; (b) large multinucleated cells with fine vacuolation in a small-celled very vascular background; (c) a predominantly large cell tissue with abnormal mitotic figures and (d) a highly malignant picture with multinucleated monstrous cells, many with grossly granular cytoplasm (figs. 179, 180, 181 & 182).

Though no fat staining was possible the tumour suggests a liposarcoma of typically abnormal structure.

For comparison with the macroscopic appearance of this tumour, a benign cystic fibroadenoma is shown (figs. 177 & 178) from a woman aged 29, alive and well 2 years 7 months after local excision.

Case 55.

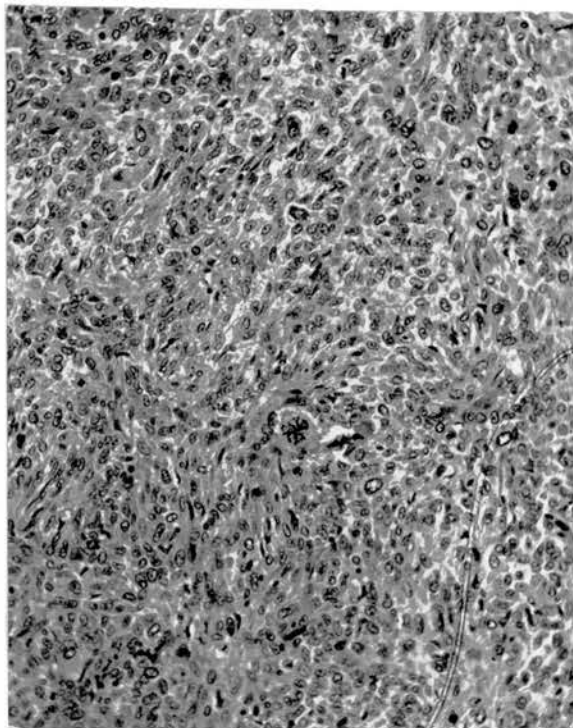


Fig. 179.

x 150

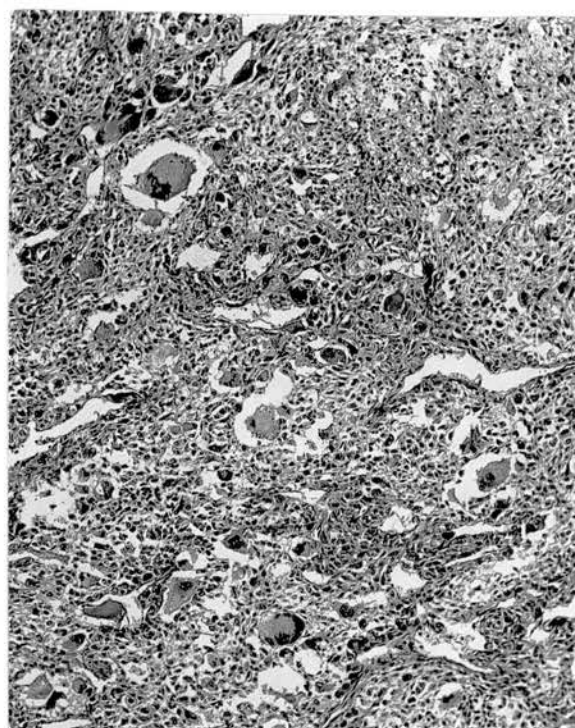


Fig. 180.

x 65.

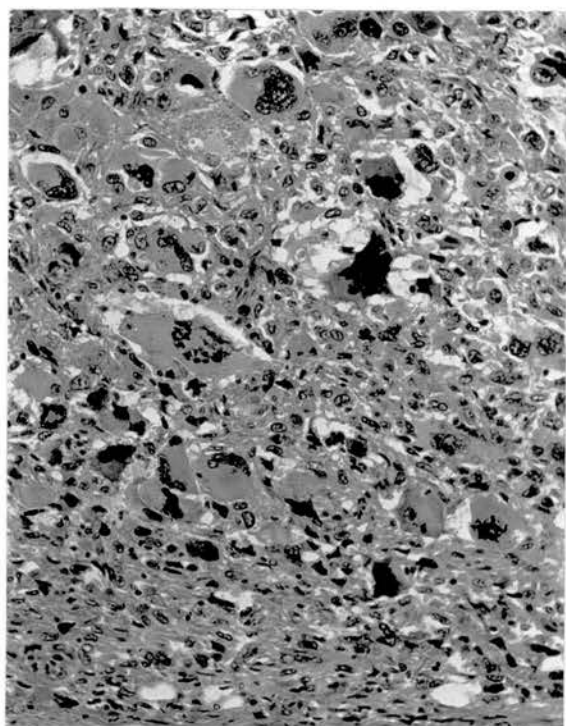


Fig. 181.

x 150

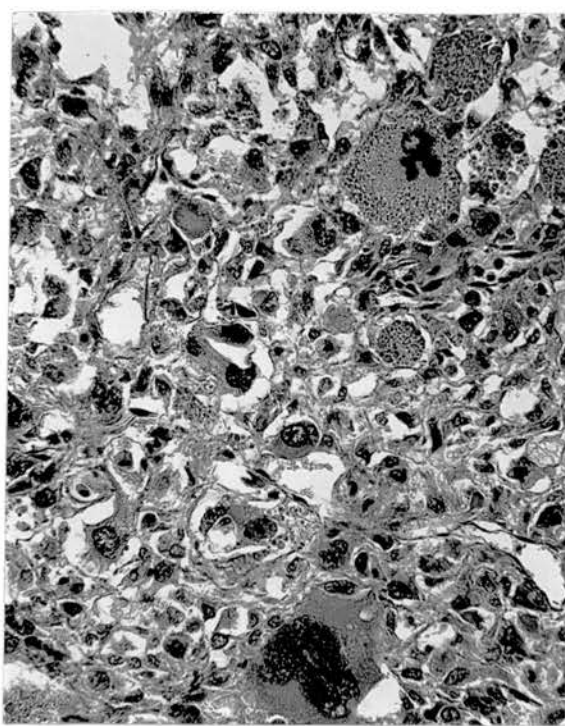


Fig. 182.

x 225.

Cases with limited data and illustration.

Case 56.

S.95.

The return of the section of this mammary tumour in a woman aged 23 years had been requested before any photography was available. This rough drawing of a small area at high magnification shows the cellular structure of a highly pleomorphic liposarcoma with monstrous cells and nuclei, many cytoplasmic vacuoles and 3 mitotic figures (fig. 183).

Case 57.

1401.

Recurrent liposarcoma in a woman aged 64 years, to show persisting lobulation and sharp demarcation of myxoid areas (right) from a fibrolipomatous area with mature fat cells (fig. 184).

Case 58.

S.146.

History: The patient, aged 56 years had noticed a tumour in the breast for 6 months.

Examination: A large mobile growth suggested "Brodie's tumour" but as X-rays showed lungs already invaded, only a local excision was done.

Histology: A fibrolipomatous structure with included small ducts and fat cells of varying size (fig. 185), in a small-celled background. Another area shows transition to a more cellular growth of less differentiated type with considerable mitotic activity (fig. 186). The tumour was fatal but date of death was not sent.

Liposarcoma in other tissues is comparable to that in the breast.

Case 59.

23.4.

The primary and the autopsy tissues of a lipomyxosarcoma of the thigh, a common site, are illustrated.

The primary tumour in a woman of 44 years of age shows an unusual mixture of liposarcoma and myxoid tissue with pools of mucus (fig. 187). It recurred in situ and after a second recurrence, unaffected by irradiation, it spread into the pelvis and a hind quarter amputation was done, but the continued spread of lipomyxosarcoma was fatal, 10 years after the initial operation. Fig. 188 shows an area of spread beyond the pelvis, with differentiation to a purely lipomatous tissue type in the perirenal extension.

Case 56.

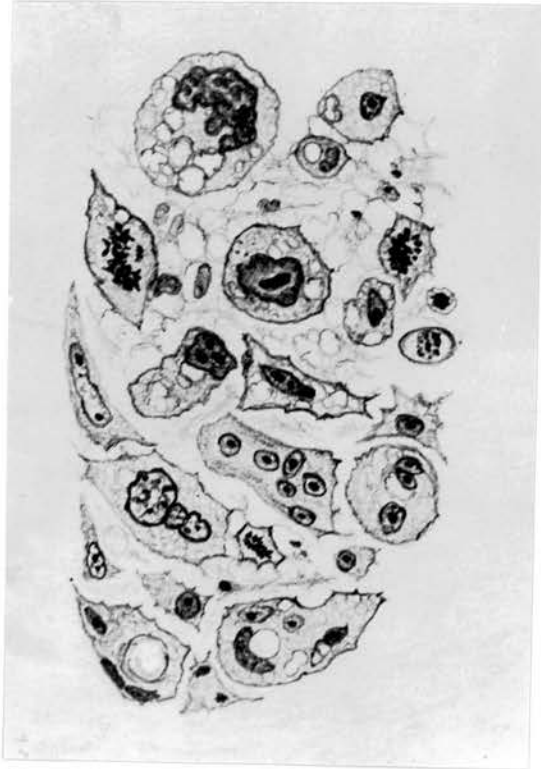


Fig. 183.

x300

Case 57.

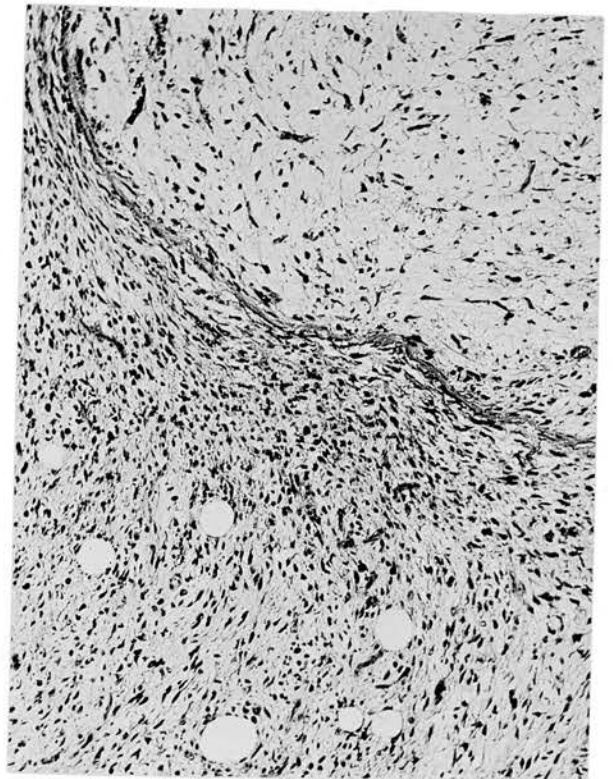


Fig. 184.

x75

Case 58.

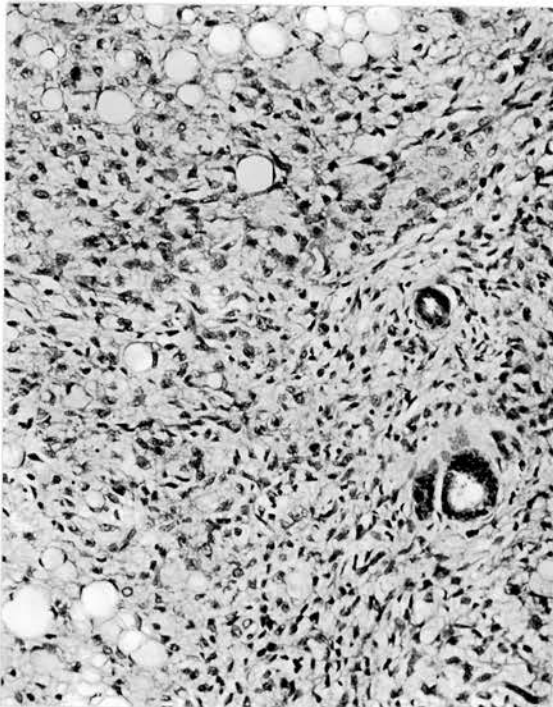


Fig. 185.

x140

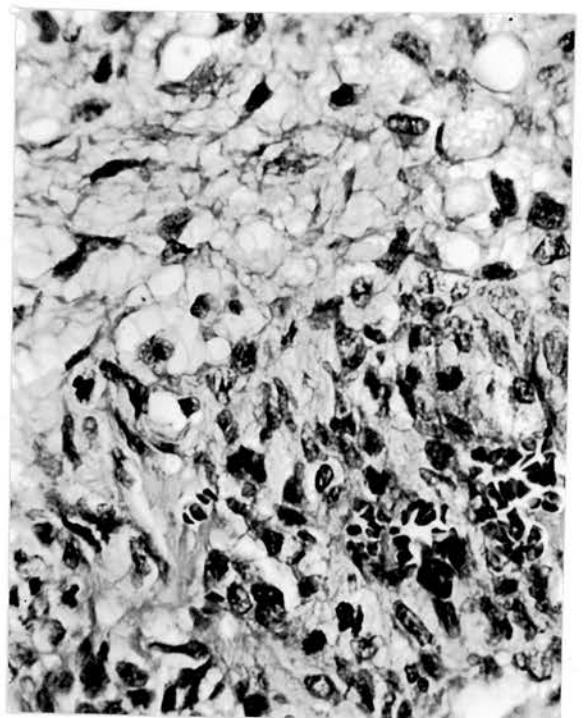


Fig. 186

x425

Case 59.

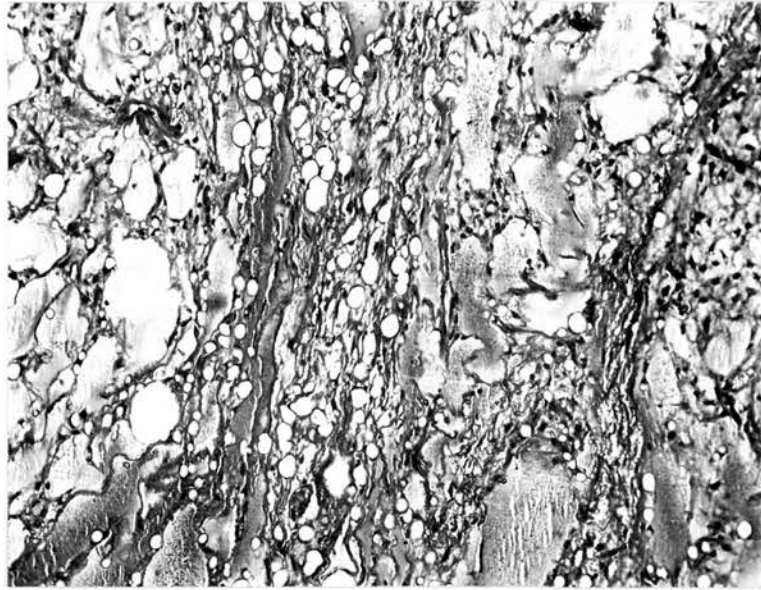


Fig. 187.

×130.

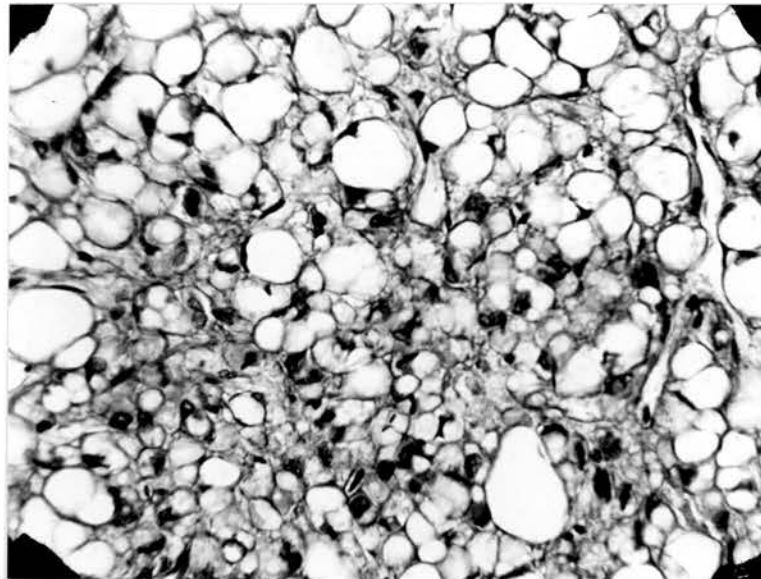


Fig. 188.

×200.

HAEMANGIOSARCOMA

Cases 60 - 69. Figs. 189 - 219.

HAEMANGIOSARCOMA

Haemangiosarcomas (malignant haemangioendotheliomas in Stout's terminology) are, from the outcome of recorded cases, the most malignant of all mammary sarcomas, and almost invariably fatal. Mackenzie (1961) analysed the 20 "fully documented and acceptable cases" from Borrmann (1907) to Shore (1957). He added a case of his own, well illustrated and with an arteriogram which confirmed its vascular origin. All these cases were eventually fatal, the survival period ranging between 2 months and 66 months. Of these 20 cases, no fewer than 9 were initially diagnosed on the histological appearances as benign. This emphasizes the difficulty of correct interpretation of the histological picture.

Three cases of mammary haemangiosarcoma are presented in this study. Stout in 1943 defined the criteria for the histological diagnosis of this rare tumour. These are (a) the proliferation of anastomosing capillaries, (b) the redundant endothelium forming a multilayered lining usually with cellular buds projecting into the lumina, (c) the frequent combination of vessels of normal and cavernous calibre and (d) the structural pattern of both vascular and solid areas. The demonstration of these features by silver staining is considered essential.

An additional case examined shows a tumour of different pattern, a haemangiopericytoma, with proliferating blood vessels separated by a cellular matrix of rounded and fusiform malignant cells, considered to be of primitive endothelial nature. This example, as illustrated in the plates, was also recurrent with blood-borne emboli and metastases.

Identical primary tumours occur in a variety of sites and have been personally examined from the skin, the heart and pericardium and the liver. Unusual findings were a haemangiopericytoma in a malignant cartilaginous salivary gland and a similar structure in part of a bony tumour of the breast illustrated in the Osteo- and Chondromatous group.

Comparable tumours are found also in animals illustrated here in a metastatic deposit of haemangiopericytoma in the liver of a dog. The congenital haemangiomatosis of fowls is very similar in structure to the human malignant type but its fatal outcome is associated with internal haemorrhages rather than with metastatic deposits.

Haemangiosarcoma

| Series | Reference | Age | Duration of tumour (years). | Type | Nodes | Therapy | Outcome in years. | Metastases |
|--------|-----------|-----|-----------------------------|---------------------|-------|------------------------------------|----------------------------------------------|----------------------|
| 60. | 1277 | 61 | 6/12 + | Angiosarcoma | - | Small biopsy. Irradiation. | Died 10/12. | - |
| 61. | 1352 | ? | 2 ⁶ /12 | do. | - | Repeated excisions and irradiation | Died 3. | Lung and bones. |
| 62. | S.172 | 86 | 3/52 | do. | - | Local excision. | Died 3 ² /12. | - |
| 63. | S.114 | 26 | 1. | Haemangiopericytoma | - | Repeated excisions and irradiation | Recurrence 14/12 Died 2 ¹⁰ /12 | Ribs and mediastinum |

For Comparison

| | | | | | | | | |
|-----|-------|----|---------------------------------------------------------|---------------------------------------------------------------------------|---|------------------------------------|---------------------------------|----------------------------|
| 64. | 44. | 64 | Varicose veins 20 yrs. | Haemangiosarcoma of leg. (Malignant granulation tissue sarcoma). | - | Amputation of leg. | Died 1/52 | Stomach and jejunum. |
| 65. | 1469. | 30 | ? | Benign angioma | - | Local excision | - | - |
| 66. | 109. | 25 | 3/12 | Capillary angioma | - | Local excision | - | - |
| 67. | 24 | 27 | 12/12 after similar tumour excised | Angioma of lower lip. (Pericytoma type). | - | Local excision | - | - |
| 68. | 704. | 56 | ? | Haemangiopericytoma | | Salivary gland tumour excision. | Recurrence with embolism. | - |
| 69. | 1400. | | Fowl with congenital angiomatosis. Tumour also in lung. | | | | | |

Case 60.

1277.

History: Patient aged 61 years noted swelling in her right breast but delayed examination for 6 months.

Examination showed a tumour of 11 cm. diameter occupying the whole of the lower half of the right breast and the greater part of the upper half (figs. 189 & 190). The nipple was slightly retracted and the skin over the tumour showed some fixation. Near the inframammary sulcus there was a well-defined reddened area of skin which had the appearance of a capillary haemangioma of recent origin (fig. 190). The tumour was completely fixed to the pectoral muscle and to the ribs. There were no palpable lymph nodes and films of her chest, lumbar spine and pelvis were negative. The growth was considered a sarcoma.

The surgeon attempted to excise the tumour but because of profuse haemorrhage and adherence to the ribs, removal was impossible. She was treated by megavoltage radiotherapy but response was poor. Her general condition rapidly deteriorated and towards the terminal stage of the disease multiple "bruises" developed on the legs and arms with pain in the back. She died at home 10 months after the first examination. There was no autopsy.

Histology: Only two small fragments of tumour tissue were available for examination. They show malignant angiomatous structure with anastomosing dilated blood channels lined by irregularly proliferating endothelium well demonstrated by the reticulin stain (fig. 192), with occasional mitotic figures. There was also gross haemorrhage with telangiectasia (fig. 191). No mammary gland tissue was seen.

Case 60



Fig. 189



Fig. 190



Post-Operative (Removal impossible)

Case 60.

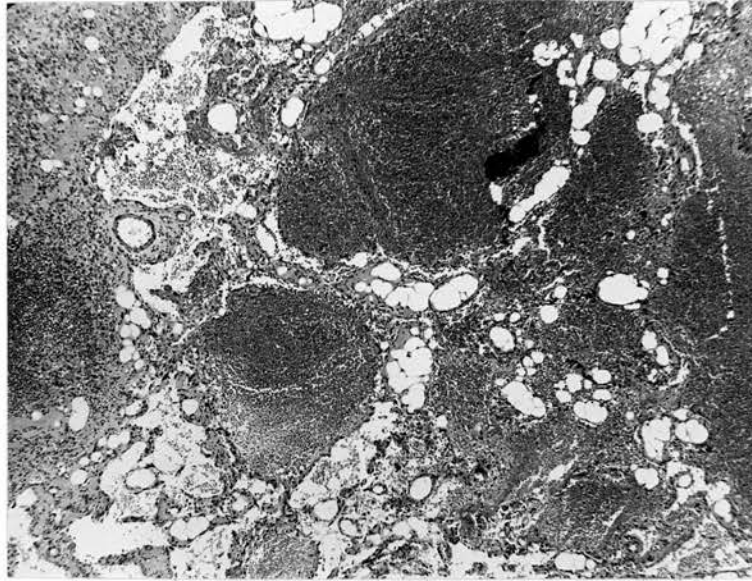


Fig 191.

x45.

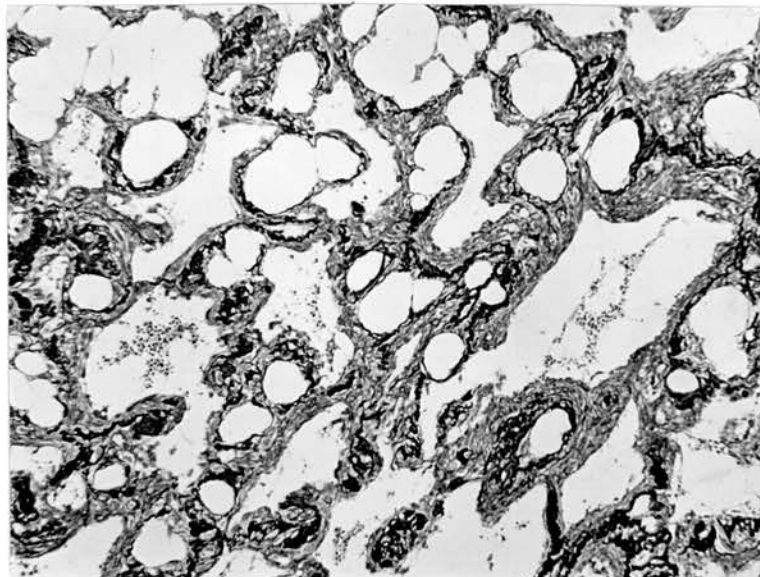


Fig 192.

x100

Case 61.

1352.

History: The first tumour in the breast was excised in 1964 and diagnosed as benign. A large "recurrence" was removed in 1965 in another hospital. In 1966, the excision of three further skin deposits was followed by radiotherapy but 6 months later she was admitted to hospital with pleural effusion and bone metastases and died a few days later, about 3 years after the first examination.

Histology: The tumour shows patches of congested capillary and cavernous blood vessels closely approximated in a cellular background (figs. 193 & 194). There is invasion of the pectoral muscle (fig. 195).

Case 62.

S.172.

History: The patient, a single woman aged 86 years, complained of a lump in the upper outer quadrant of the left breast found three weeks before.

Examination showed a small hardish lump roughly the size of a walnut, irregular in outline and adherent to skin and deep tissues. There was no nipple discharge. Some discoloration of the overlying skin was visible. No nodes were palpable. Tumour and overlying skin were excised under a local anaesthetic, the tissue at operation suggesting an angiomatous condition. The patient died 3 years 2 months after operation, with a sudden cerebral haemorrhage possibly associated with the tumour condition but there was no autopsy.

Histology: The tumour, sectioned in toto, showed numerous dilated and congested anastomosing capillaries lined by swollen proliferating endothelium (figs. 196 & 197) with haemorrhage in some areas (fig. 198). The general tumour structure is well shown in the reticulin-stained area (fig. 199).

This is a characteristic haemangiosarcoma (figs. 196 & 197), not unlike Kaposi's sarcoma, which is now generally regarded as a similar malignant condition.

Case 61.

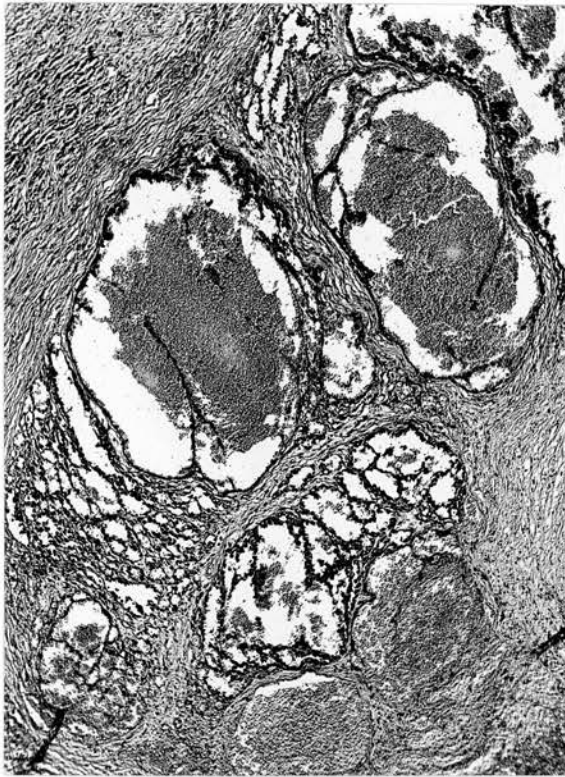


Fig. 193.

x 50

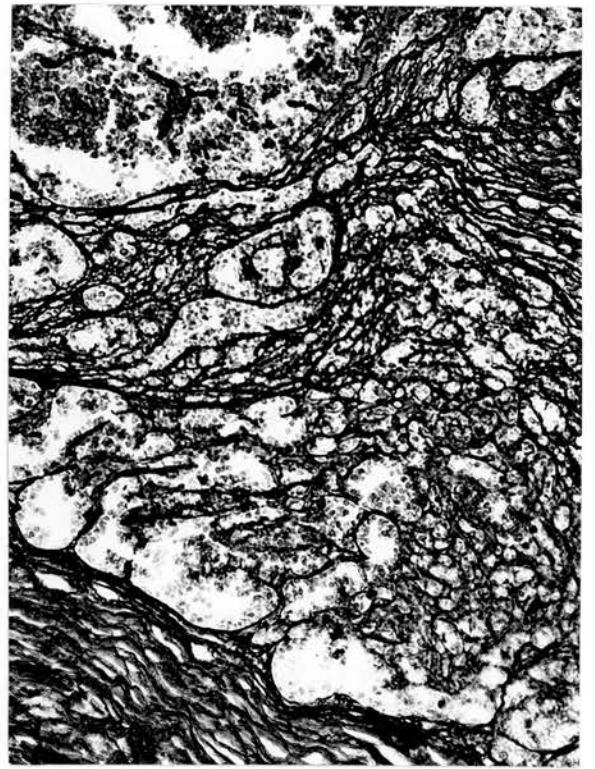


Fig 194

x 225

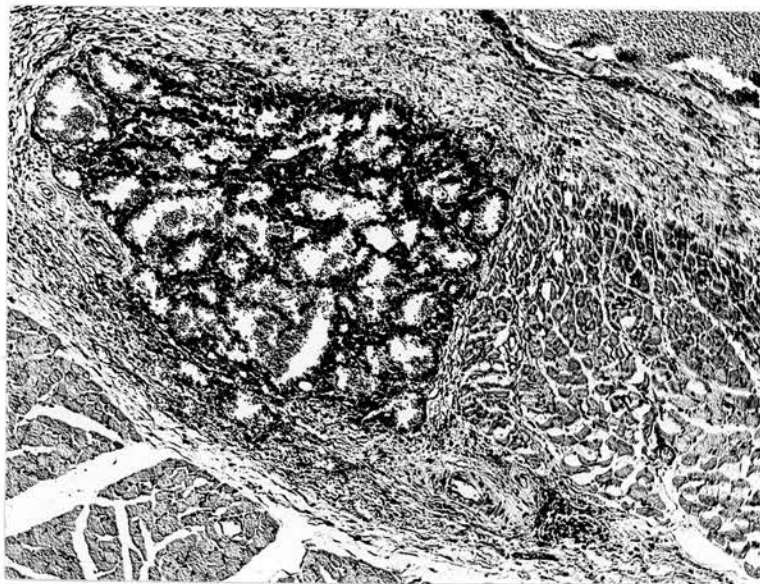


Fig 195.

x 75.

Case 62.

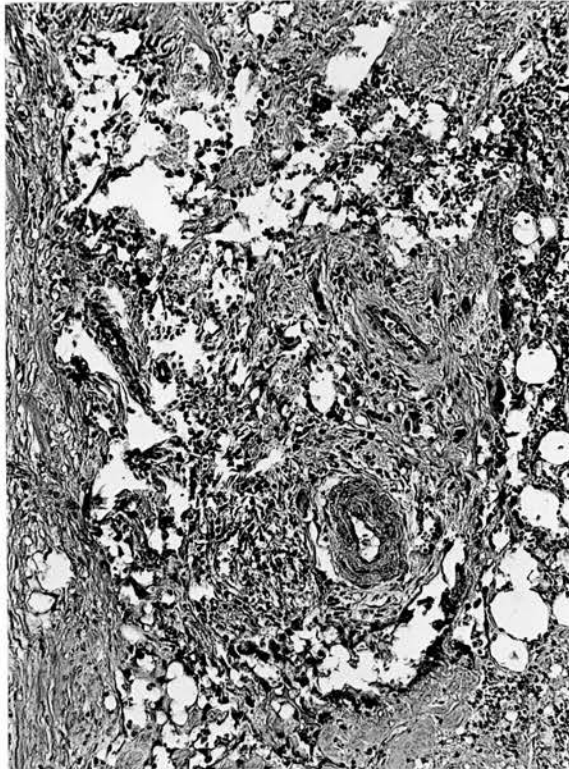


Fig. 196

x 100.

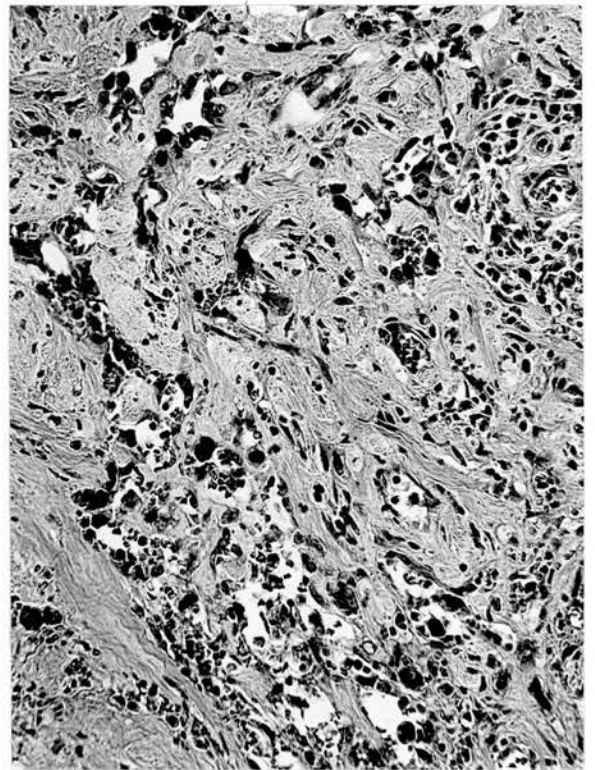


Fig. 197

x 225

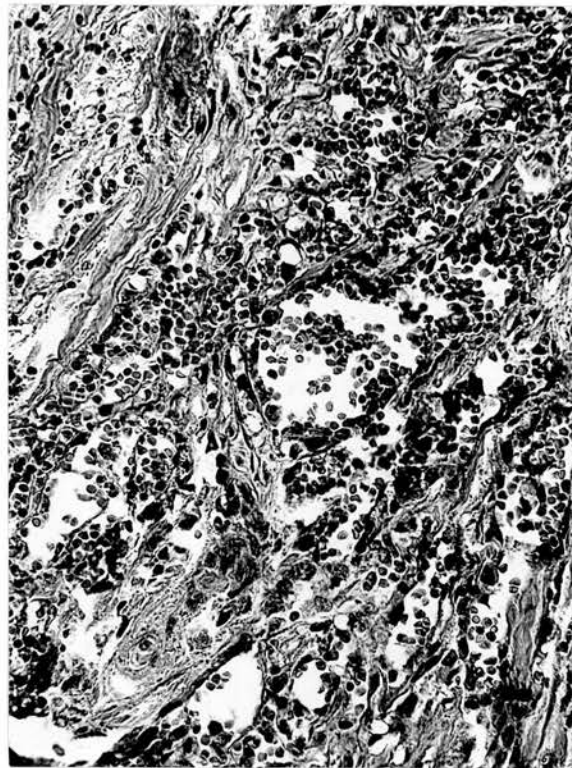


Fig. 198

x 250

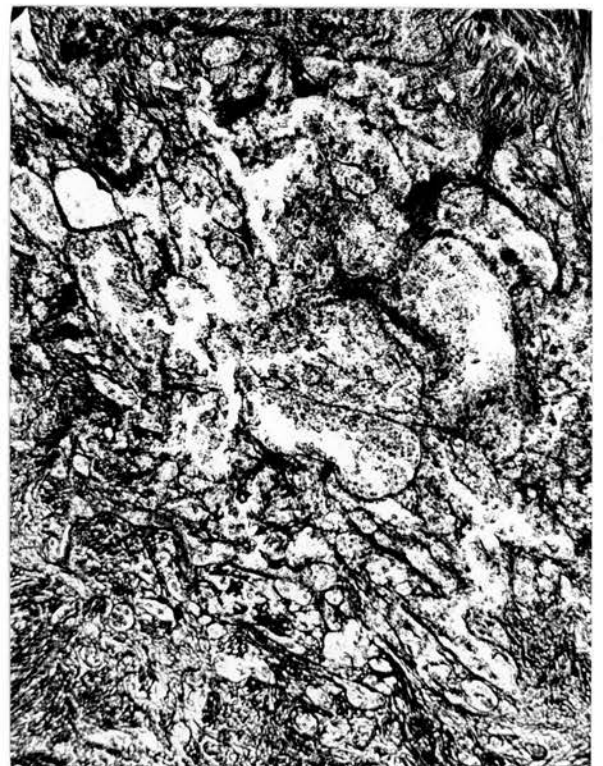


Fig. 199

x 100.

Case 63.

S.114.

History: The patient, aged 26, had noticed a lump in the breast for a year.

Examination showed a mass in the left breast attached to intercostal spaces, and suggestive of haemangioma. The tissue excised was about 4 x 2.5 cm. rather ill-defined and with a trabecular structure in which were many small cavities, some filled with blood. The tumour recurred in situ 14 months later, noticed by the patient for 6 weeks and associated with a trauma. Her general health was good. The recurrence, 2.5 cm. in diameter, was soft, pinkish and ill-defined with infiltrating fingers of tumour spreading into muscle. Repeated local recurrences were later excised and the area irradiated but further infiltration involved the ribs and mediastinum. The patient died 2 years 10 months after the first operation.

Histology: The general architecture of the primary growth is shown in an enlarged view of the tumour section (fig. 200). The vascular channels of very varying calibre show little or no endothelial proliferation but are surrounded by a closely cellular tissue of isomorphic rounded and polygonal cells, with numerous mitotic figures (figs. 201 & 202). The recurrences and autopsy tissues were of similar appearance (fig. 203).

This is a haemangiopericytoma of Stout's description, regarded as a rare variant of haemangiosarcoma.

Case 63

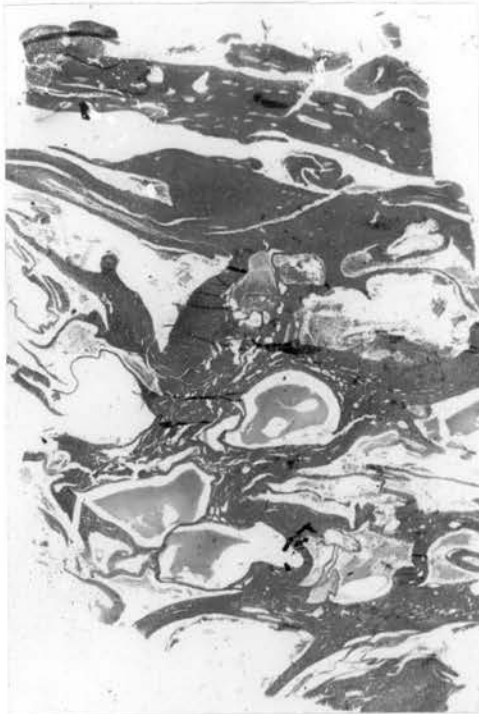


Fig. 200

x 4



Fig. 201.

x 100



Fig. 202.

x 150

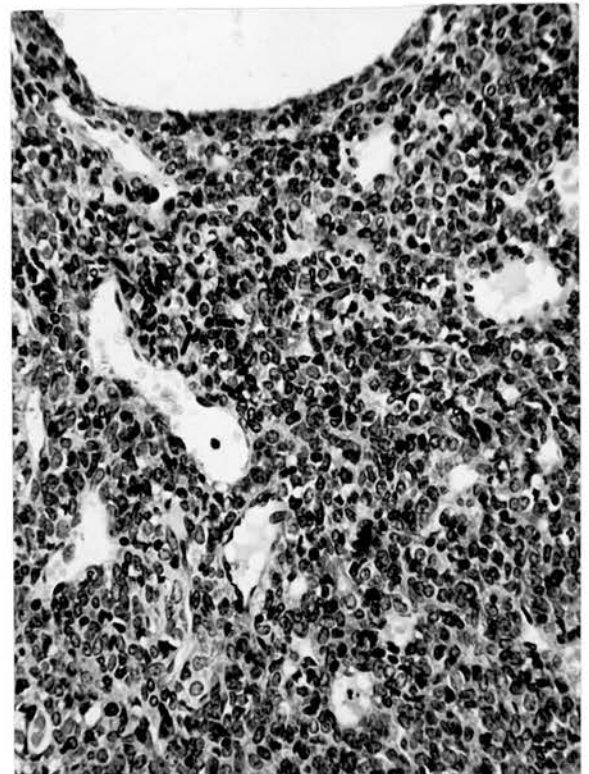


Fig. 203

x 300

Haemangiosarcoma in tissues other than mammary is shown for comparison.

Case 64.

44.

History: The patient aged 64 years had varicose veins of both legs and was in and out of hospital for 20 years, with continual breaking down and healing of the skin. One leg, because of a major trauma, did not heal.

Examination showed a large fungating growth in the ulcerated area which progressed in size and depth, with much haemorrhage and infection and was obviously malignant. Metastases appeared as large growths in stomach and jejunum of similar structure with a rapidly fatal outcome.

Histology: The tumour is a haemangiosarcoma. Near the skin it shows numerous anastomosing capillaries with some redundant endothelium (fig. 204). At a deeper level the closely-set vessels tend to form sheets of spindle cells, with recognisable capillaries mainly peripheral (fig. 205), but the vessels in all areas are outlined by the reticulin stain (fig. 206). A high power view shows the anastomosing blood channels lined by an excess of endothelial cells and numerous mitotic figures (fig. 207).

This is an instructive case of haemangiosarcoma, sometimes called malignant granulation tissue sarcoma or malignant granuloma. It is a very rare tumour, originating in a non-healing injury of long-standing or in an unresolved haematoma (Pack & Ariel, 1958).

The amputated limb is a specimen in the Museum of the Royal College of Surgeons of Edinburgh.

Case 64.

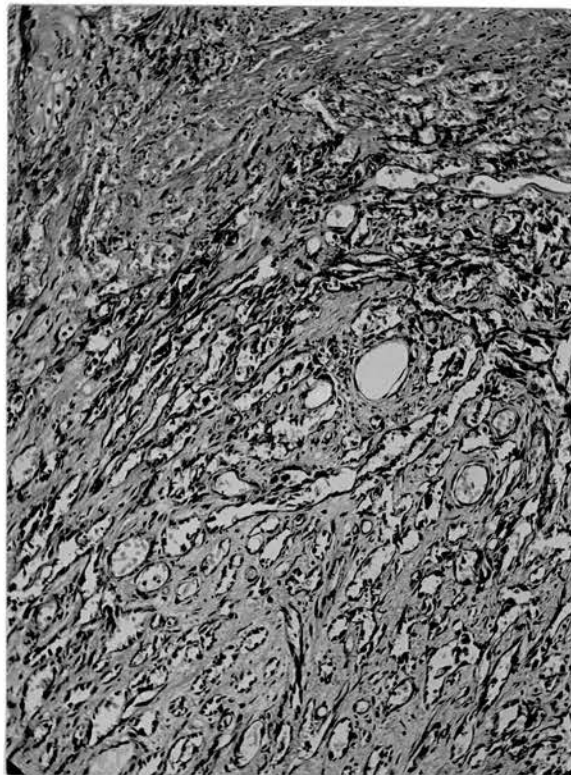


Fig. 204.

x 100

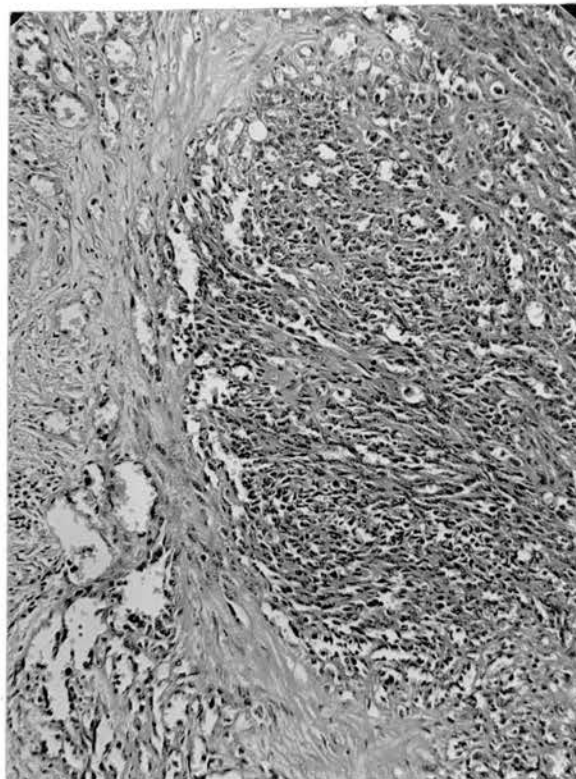


Fig. 205.

x 120

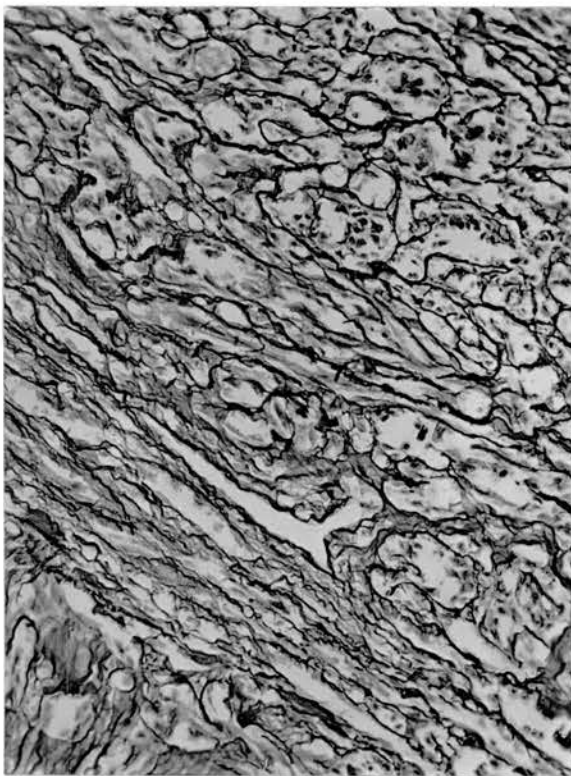


Fig. 206

x 200

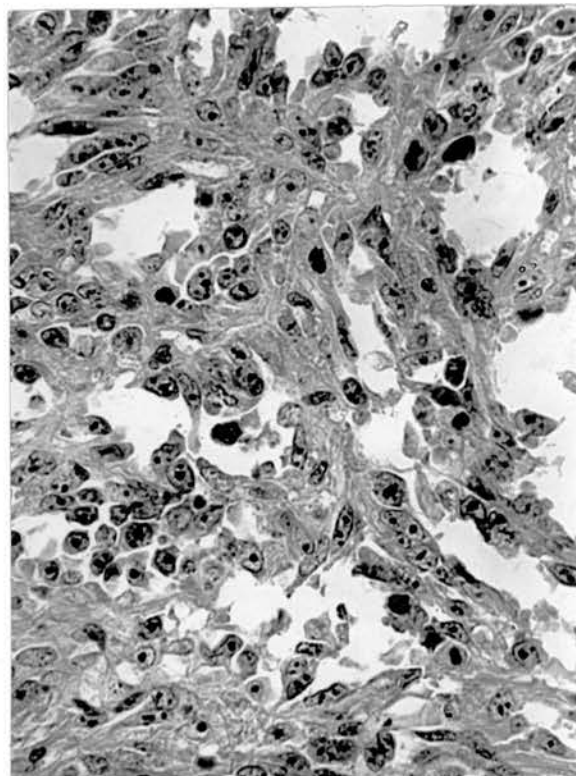


Fig. 207.

x 425.

Case 65.

1469.

This benign angioma was excised from the breast of a patient aged 30 years. It shows dilated capillaries, some with blood contents. Though there is vessel anastomosis no endothelial cell proliferation is present (fig. 208).

Case 66.

109.

A capillary angioma of the skin of the breast from a patient aged 25 years shows a much more cellular structure. The other breast 3 months previously had developed an abscess during lactation and the present tumour, diagnosed as a "milk cyst", was found when the abscess was opened. There is no evidence of malignant change in the second breast though the tumour extends from skin down to and into pectoralis major, with fixation. Tumours of this type may raise clinical and operative difficulty (fig. 209), but do not recur if adequately excised.

Case 67.

24.

This angioma of the lower lip occurred in a woman aged 27 years. It suggested a cyst and a similar condition had been removed a year previously. This small circumscribed angioma was below and independent of the epidermis. The structure is of anastomosing blood vessels with the proliferating cells lying mainly between them, indicating an angioepitheliomatous picture rather than haemangioma (figs. 210 & 211).

Case 65

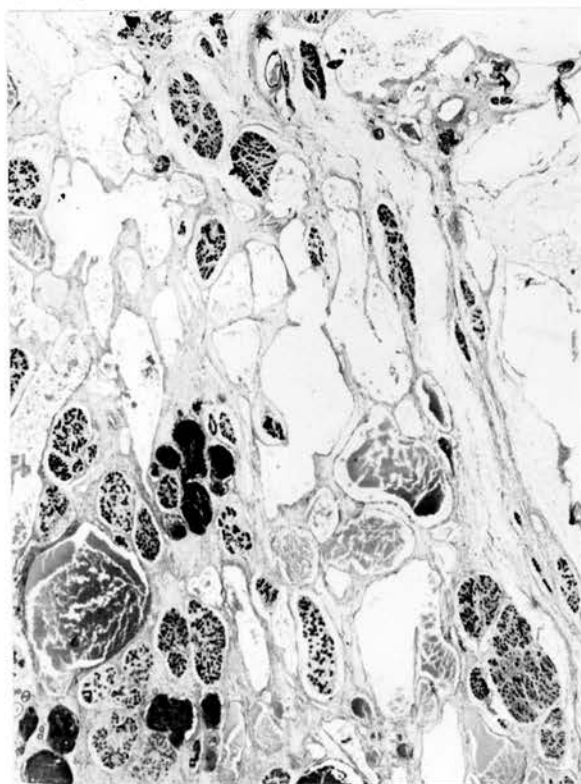


Fig. 208

x30

Case 66

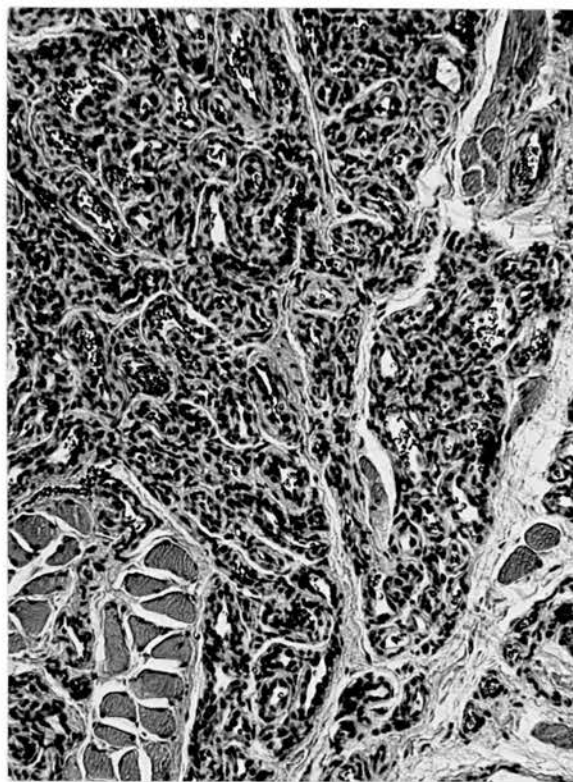


Fig. 209

x150

Case 67.

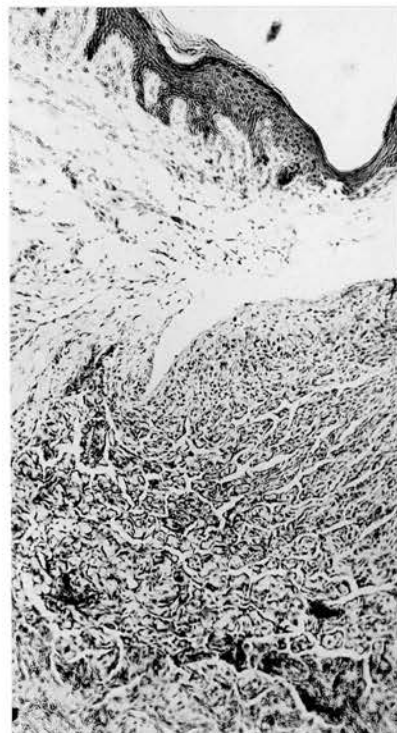


Fig. 210

x40

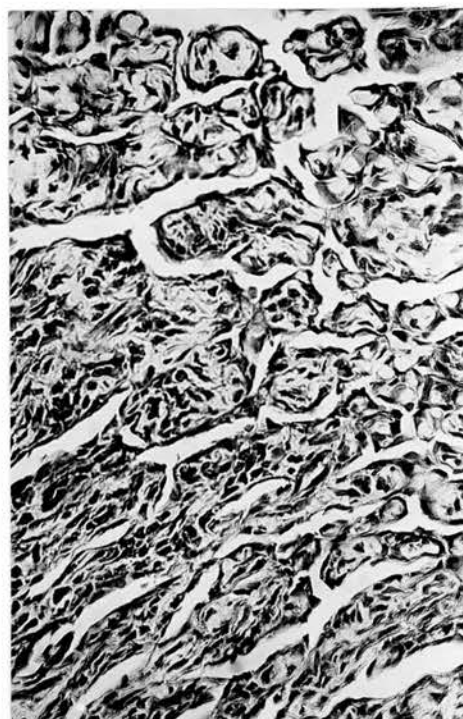


Fig. 211.

x150

Case 68.

704.

History: The patient aged 56 complained of a tumour in the mouth.

Examination showed a lobulated tumour 5 x 2.5 x 2.5 cm. It extended from the right tonsil with the upper pole half above the hard palate. At operation it shelled out easily and did not suggest malignancy and it healed well. A small growth in the parotid region was removed 13 months later but there was no further trouble for 5 years 5 months when an ulcerated area appeared on the same side of the palate but did not suggest tumour. Five months after removal, the condition indicated a slow recurrence but the patient did not report again and has not been traced since. The initial tumour is shown as a stained section (fig. 212).

Histology: The structure is unusual but areas show some comparison with figs. 105 and 202. No mucous gland tissue is seen in any of the areas shown. Fig. 213 shows cartilage calcified and non-calcified separated by a hyaline zone; fig. 214, an area of early cartilage and, on the right, a very cellular pericytoma tissue; fig. 215, the pericytoma pattern on the left, being obscured by cartilage formation on the right; fig. 216, the typical pericytoma structure emphasized by Masson's Trichrome stain. The recurrent tumour was entirely angiomatous (fig. 217) and shows a more cellular pericytoma structure with irregular dilated capillaries and is more actively mitotic. Fig. 218 shows massive invasion of a dilated blood vessel by undifferentiated cell masses.

Though the patient was later untraced there is little doubt the condition was eventually fatal as the outcome almost invariably is in malignant blood vessel tumours.

Case 68

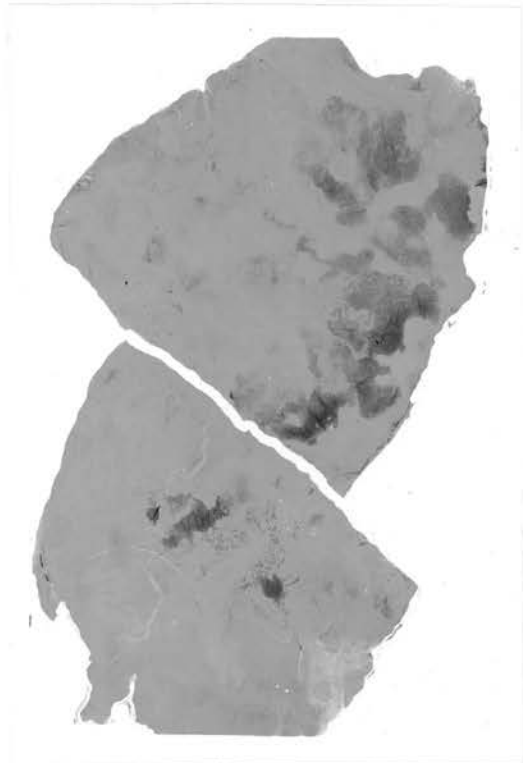


Fig. 212

x3

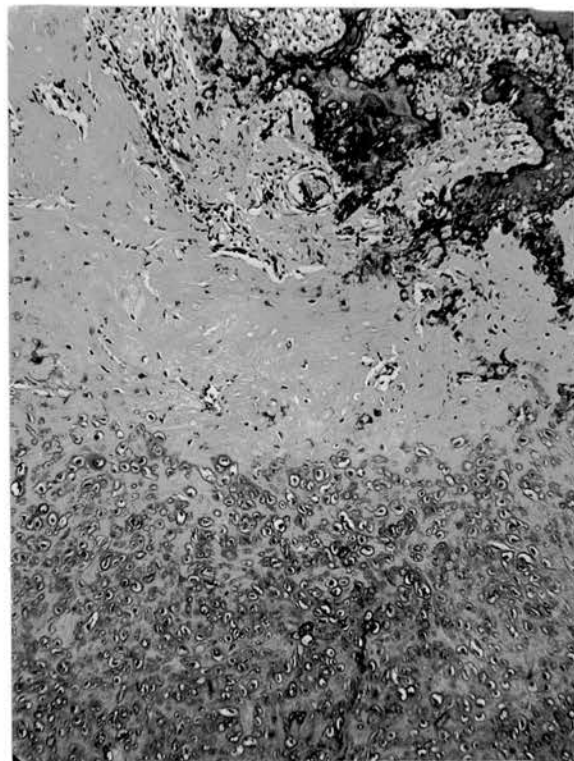


Fig. 213.

x100



Fig. 214.

x100.

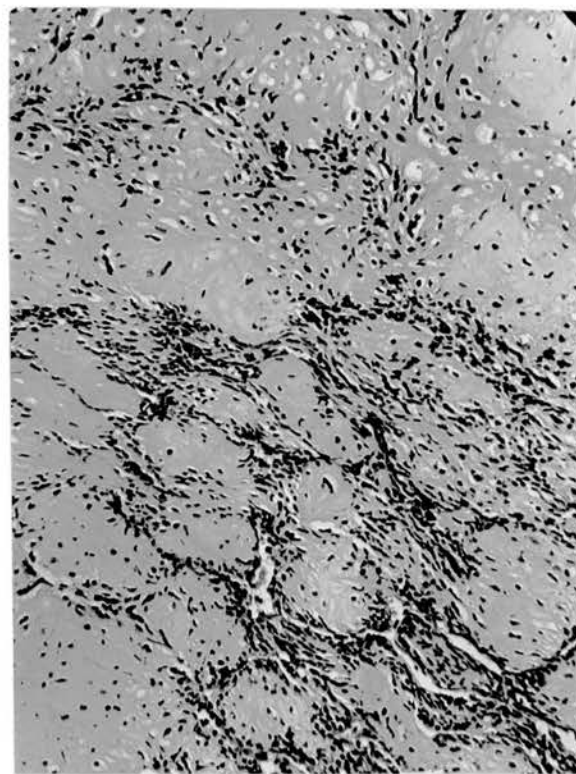


Fig. 215

x150.

Case 68

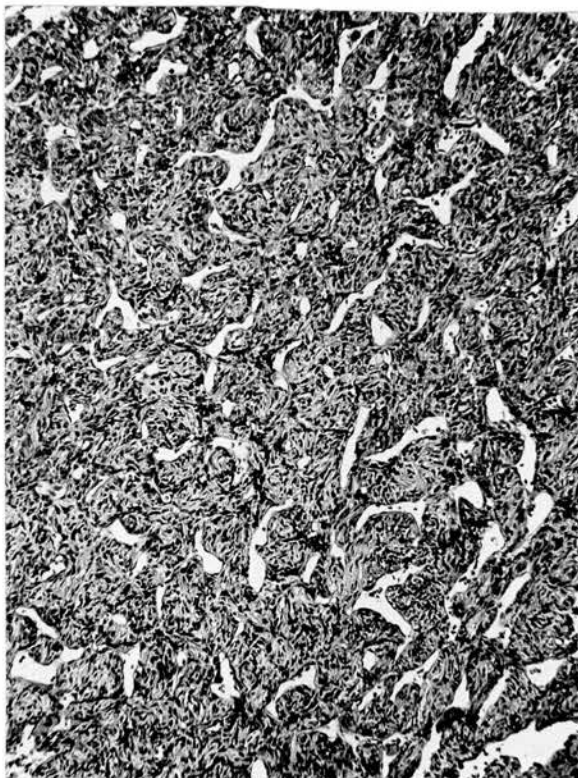


Fig. 216

x 100

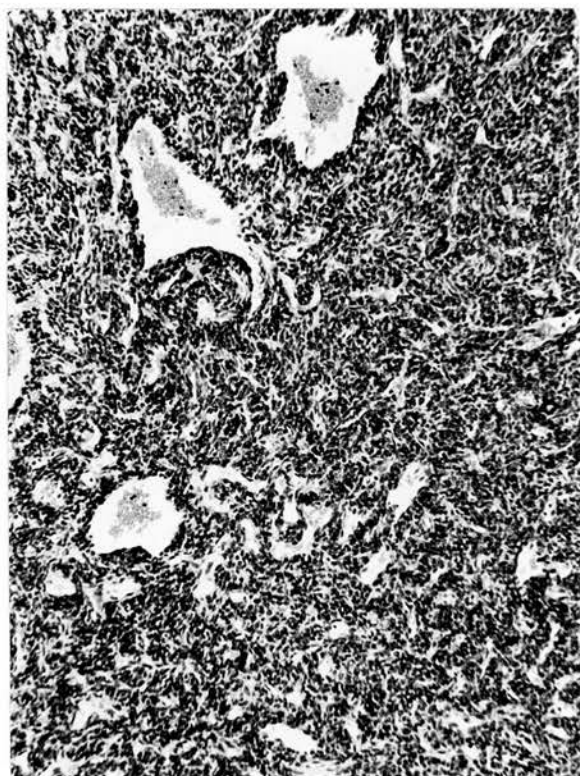


Fig. 217.

x 100

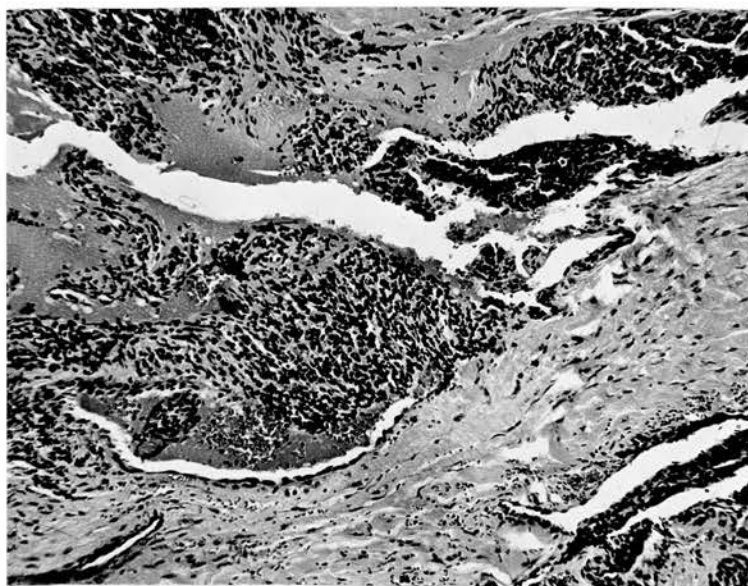


Fig. 218

x 100

"Post mastectomy lymphangiosarcoma" arising in lymphoedematous arms lies outside this study of mammary sarcomas. It has been dealt with in many reports since Stewart and Treves' initial description and more recently and critically by Salm. The few angiosarcomas described here are primary blood vessel tumours of the breast unconnected with any previous mammary carcinoma. The over zealous clearance or treatment of the axilla in mammary cancer cases, with obstruction and destruction of lymphatic channels, could theoretically lead to regenerative proliferation of these vessels and therefore possibly to lymphangiosarcoma. A similar process is seen in the proliferation of capillaries which may in longstanding cases lead to haemangiosarcoma, as illustrated in case 64 briefly described and illustrated here.

Case 69.

1400.

(Figs. 219 a, b & c).

a. The skin of a fowl with congenital haemangiomatosis.

The structure is very similar to the human angiosarcomatous pattern already described (figs. 194 & 195). It shows anastomosing blood vessels lined by endothelium with considerable proliferation. The blood content is emphasized by the nucleated avian red cells. In fowls, the condition is usually considered a benign multiple focal proliferation of blood capillaries but a proportion shows histological features which could be interpreted as evidence of malignancy (Campbell).

Blakemore and Innes (1931) think them actively neoplastic, invasive and locally destructive. This, in human cases, used to be called "benign metastasizing haemangiomas" (Shennan 1914).

b. A similar picture in the skin of a fowl.

c. A third example, with dilated capillaries and cellular structure resembling the haemangiopericytoma type, comparable with the human case shown in figs. 202 & 203.

Case 69.

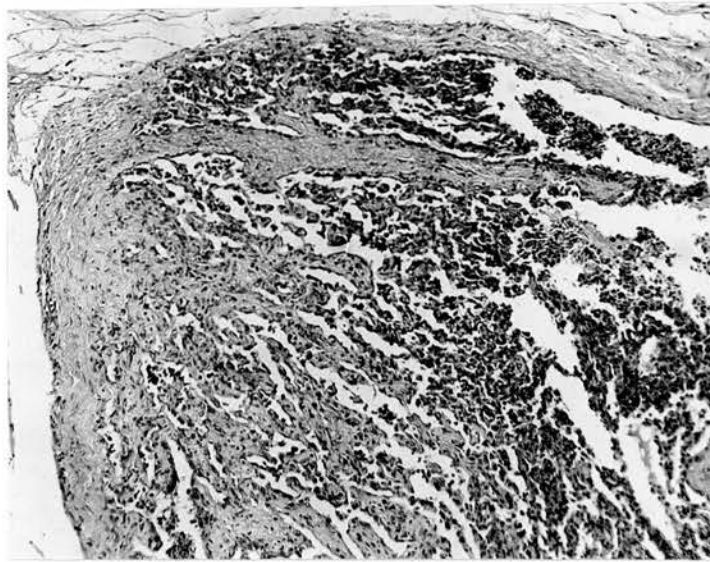


Fig. 219.a.

× 80.

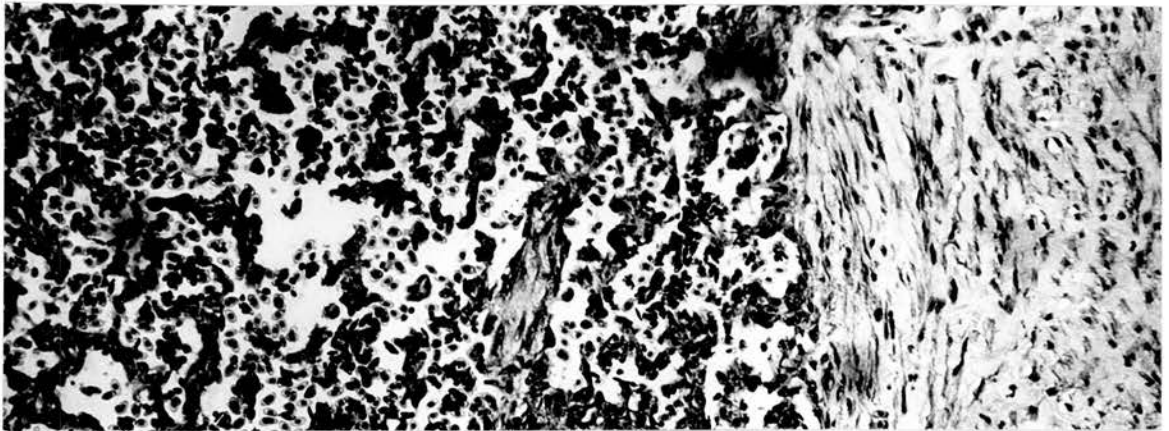


Fig. 219.b.

× 135.

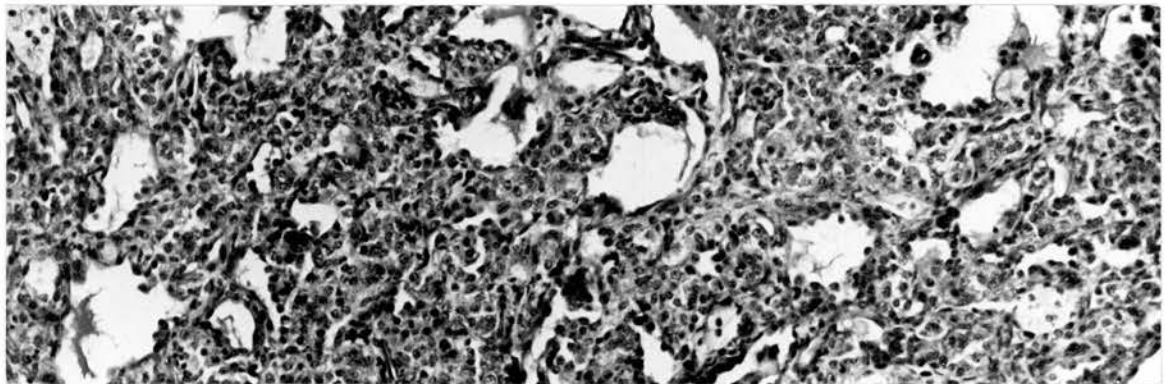


Fig. 219.c.

× 135.

SARCOMA IN THE YOUNG

Cases 70 - 73. Figs. 220 - 228.

Mammary Sarcoma in Young Subjects

Four cases of exceptional interest by reason of the very young age of the patients warrant separate study.

The four patients were aged between 19 and 23 years. If it is accepted that the majority of mammary sarcomas have their genesis in a simple fibroadenoma, intra- or pericanalicular, then the period of transition from innocent to malignant tumour must have been exceptionally brief. This contrasts with the average age incidence of breast sarcomas which is some 3 or 4 decades later and in such patients the antecedent history of the presence of an innocent breast tumour often extends over many years.

These patients all became pregnant after the original operation and all had fatal recurrence of the disease subsequently. That pregnancy has a deleterious effect on mammary carcinoma is established (Dawson 1935) but no evidence has previously been put forward suggesting that a similar relationship may exist with the growth of sarcomas.

Fibrosarcoma - Young Patients

| Series | Reference | Age | Duration of tumour. (years). | Type | Nodes | Therapy | Outcome in years. | Metastases |
|--------|-----------|-----|------------------------------------|------------------------------|-------|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|-------------|
| 70 | S.106 | 19 | 6/12 | Fibroadenoma into sarcoma | - | Local excision | Recurrence + mastectomy | - |
| 71 | S.103 | 21 | ? | Fibrosarcoma. | - | Local excision Amputation and radiotherapy. | Died | Mediastinum |
| 72 | S.137 | 23 | ? | Fibrosarcoma | - | Local excision | Recurrence Simple mastectomy. (Childbirth 1 ³ /12 post mastectomy). Alive 1 ¹⁰ /12 | - |
| 73 | S.26 | 21 | 3/12 + | Fibrosarcoma | - | Local excision and irradiation | (Childbirth 1 ⁹ /12 after mastectomy). Died. | - |

Case 70.

S.106.

History: The patient aged 19 years said a lump had been present in the breast for 6 months.

Examination: It was a fibroadenoma clinically and was locally excised. The small piece sent had been reported as such, though it had a mottled appearance.

Histology: An intracanalicular fibroadenoma in which the growth of the vascular and myxoid polyps had compressed the epithelium to little more than a thin layer of flattened cells surrounded by more active stroma (fig. 220). After 17 months, when the patient was aged 20 and married, the tumour recurred and radical mastectomy then showed transitions from a myxoid fibroadenoma with increasing fibroblastic proliferation to a very cellular small-celled fibrosarcoma (fig. 221). There were no invaded axillary nodes. The following month a small haematoma, hard and surrounded by active granulation tissue was removed from the scar but no tumour remained. No later note was available.

Case 71.

S.103.

History: The patient aged 21 years went to her doctor at once when she found a lump in the breast.

Examination: The tumour was already about 6 cm. in diameter and suggested rapid growth. It was irregular in outline, very hard in the centre, not fixed to skin or deep tissues and no axillary nodes were palpable. Local excision was done at once and the pathologist reported "endothelioma with cellular perivascular structure which must be regarded as sarcomatous". Amputation and radiotherapy followed this report. She remained well and married, but when pregnant she began to go down hill and 17 months after operation, X-rays showed extensive mediastinal secondaries. The exact date of death was not given and there was no autopsy.

Histology: This patient was treated during the early years of the 2nd World War and the additional operation tissue requested was lost in transit. No epithelial elements were recognised in the tissue examined but many non-epithelial diagnoses had been suggested. The tumour is a sarcoma with considerable perithelial structure in areas (figs. 222 & 223).

Case 70.



Fig. 220.

x 50.

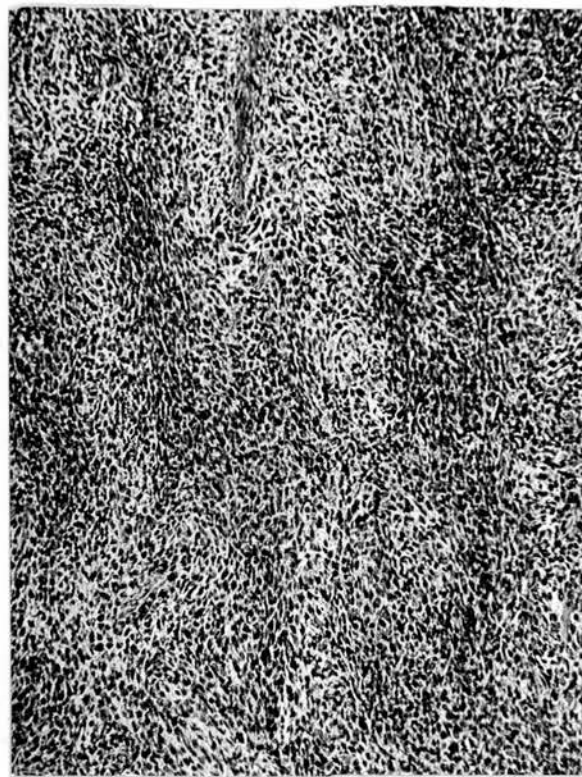


Fig. 221.

x 100.

Case 71.

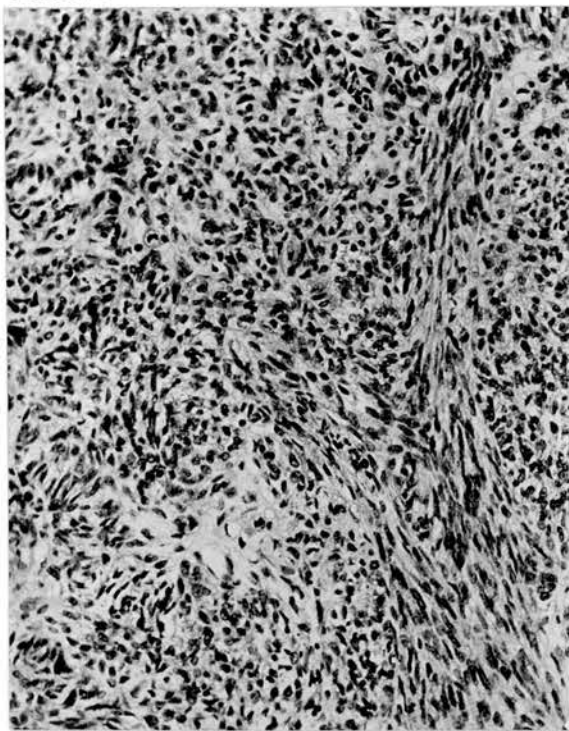


Fig. 222.

x 150.

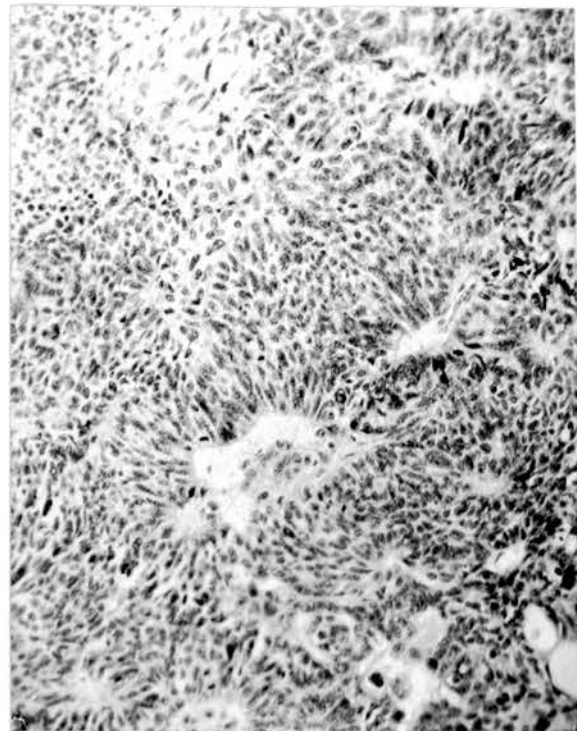


Fig. 223.

x 150.

Case 72.

S.137.

History: The patient aged 23 years had a swelling the size of a tangerine orange in the upper half of the breast of unknown duration. No axillary nodes were palpable. The tumour shelled out but recurred after 2 months and simple mastectomy was done. The first child was born 15 months after mastectomy and the patient was alive and well 3 years 1 month after the first operation.

Histology: Mammary ducts are surrounded by a cellular fibrosarcoma with mitotic figures (fig. 224). In areas without glandular remnants, very numerous mitotic figures and some cell pleomorphism are evident (fig. 225).

This tumour shows an unusual outcome, with a large primary growth and recurrence, followed by childbirth and the patient's survival over 3 years, but was eventually fatal.

Case 73.

S.26.

History: The patient aged 21 years found a small lump in the breast when about to be married and wished treatment deferred.

Examination: The tumour was diagnosed as a fibroadenoma and the patient put on a waiting list. It grew rapidly in the 3 months before it was treated by excision and irradiation. She had a child 1 year 9 months after operation and was well for some months but then developed lung metastases. The total survival time after the first examination was 4 years 5 months.

Histology: Much of the tumour shows an intracanalicular fibroadenoma with stroma of varying cellularity (fig. 226) but mainly of active growth (fig. 227). In areas of purely fibrosarcomatous tissue there is some pleomorphism with very numerous mitotic figures - over 10 in a high power field, as in fig. 228.

Case 72.

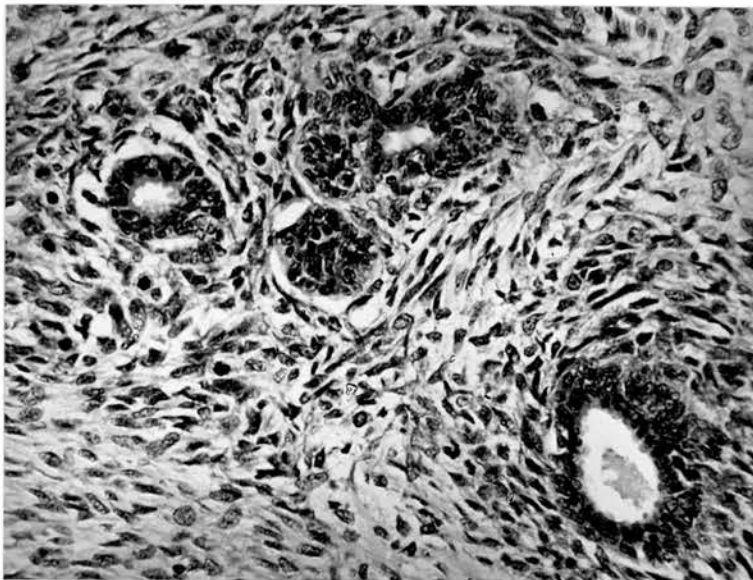


Fig. 224.

x300.

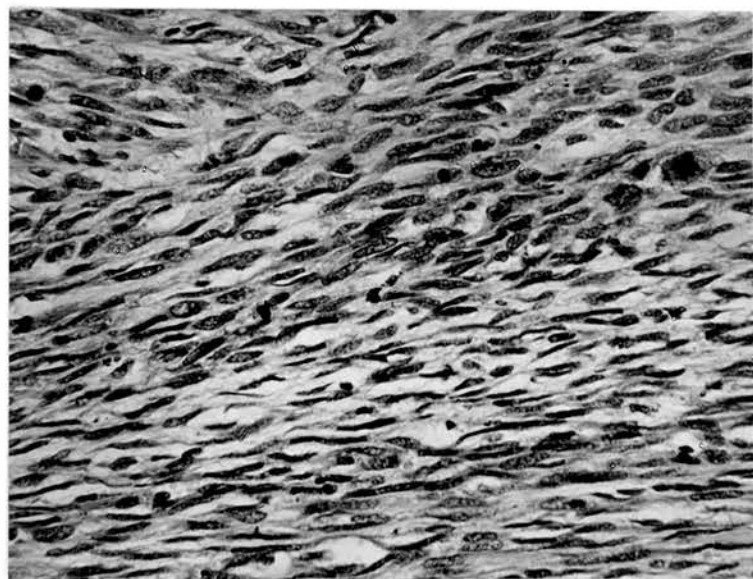


Fig. 225.

x300.

Case 73.

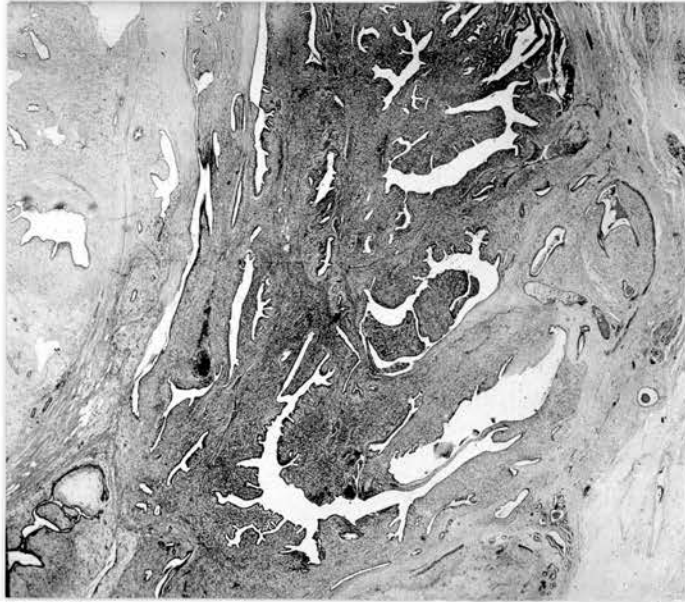


Fig. 226.

x7.5



Fig. 227

x 140

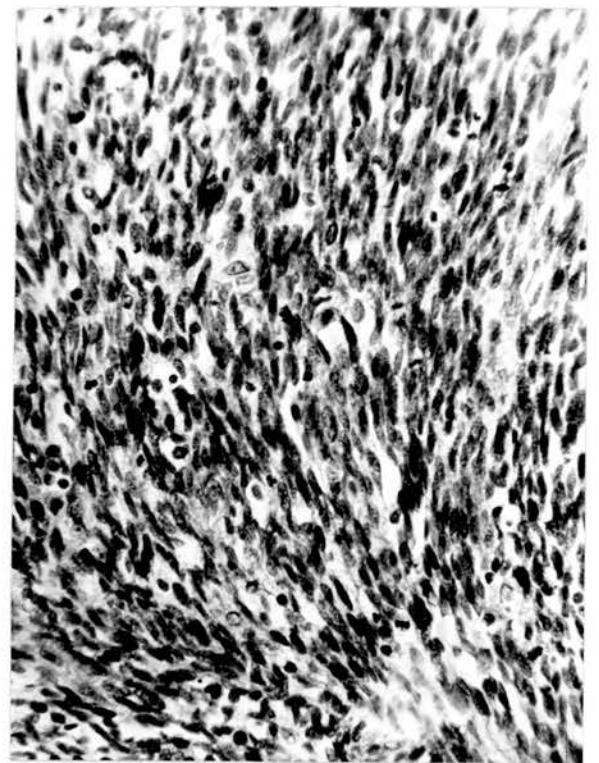


Fig. 228

x300

SARCOMA IN THE MALE

Cases 74 - 77. Figs. 229 - 234.

Mammary Sarcoma in Male

Recorded cases of mammary sarcoma in male subjects are excessively rare and justify separate grouping. Connell (1907) described a single case in a male of 25 years; he quoted earlier cases but without histological findings or later history. D'Aunoy and Wright (1930) found 4 cases in males in 57 reported sarcomas and added 1 male case among the 11 mammary sarcomas observed by them. Schreiner & Thibaudau (1932) recorded 1 male case in 7 breast sarcomas, all active fatal neoplasms of uniform spindle-cell structure.

Diffuse enlargement of the male breast, gynaecomastia, is a benign fibroadenomatosis and rarely encountered in routine reporting. Fibroadenomas are even rarer, only 4 cases having been personally examined.

In the 4 cases of sarcoma of the male breast here recorded in no instance was there any evidence of development of the malignant neoplasm from a benign precursor. Since, however, in these cases the lesion was an advanced one, it might well be that the evidence of the genesis had been obliterated.

Mammary Sarcoma in males.

| Series | Reference | Age | Duration of tumour. (years). | Type | Nodes | Therapy | Outcome In years. | Metastases |
|--------|-----------|-----|------------------------------------|----------------------|-------|-----------------------------------|----------------------------|------------|
| 74. | S.154. | 25 | 3. | Fibrosarcoma. | - | Local excision + radiotherapy. | 2 Recurrences Alive 17. | - |
| 75. | S.15. | ? | 40. | Bone in fibrosarcoma | - | ? | Died. | - |
| 76. | S.33. | 50 | 6/12. | Liposarcoma (?) | - | Mastectomy | ? | - |
| 77. | S.145. | 51. | 3/12. | Fibrosarcoma | - | Local excision. | Died | - |

Case 74.

S.154.

History: A male patient aged 25 gave a history of swelling in the mammary area for 3 years with slow increase in size. It was locally excised but recurred fairly rapidly and was again excised. A second recurrence 7 x 7 cm. in diameter followed 2 years later and was reported as a fibroma. The skin over it was reddened and the tumour was fixed to the pectoral muscle with some lateral displacement of the nipple. Wide excision with removal of the pectoral muscle and radiotherapy followed. He remains well without further recurrence for 20 years after the swelling was first noticed i.e. 17 years after the first excision.

Histology: This is a malignant growth, a fibrosarcoma, but the actual site of histogenesis is a little doubtful (Figs. 229 & 230).

Case 75.

S.15.

History: This is a very old case. The tumour was removed at autopsy from an elderly male patient where it had been present for 40 years.

Examination showed a very hard nodular growth in the breast with some patchy bone formation.

Histology: An area showed early osteoid tissue in a fibroblastic pleomorphic matrix (fig. 231). In some parts more defined bony areas are found with dilated capillaries (fig. 232).

The patient died in 1824 and good photomicrography was difficult.

Case 74.

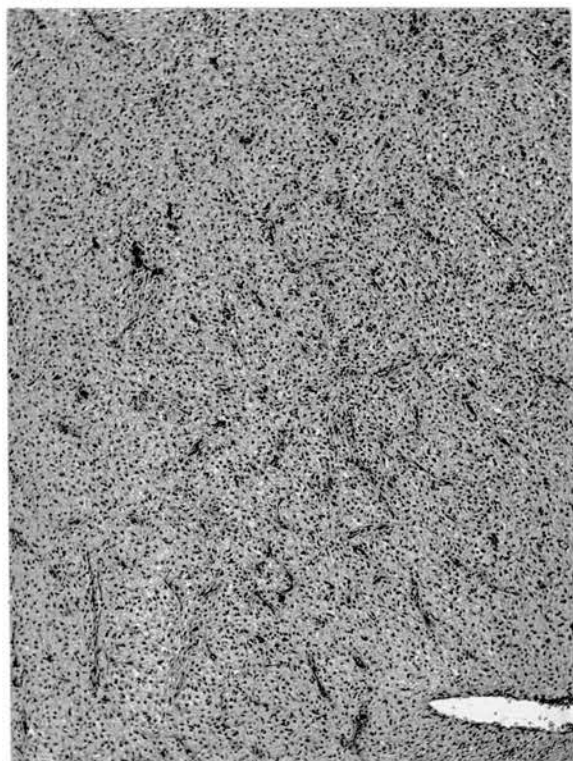


Fig. 229.

x 50

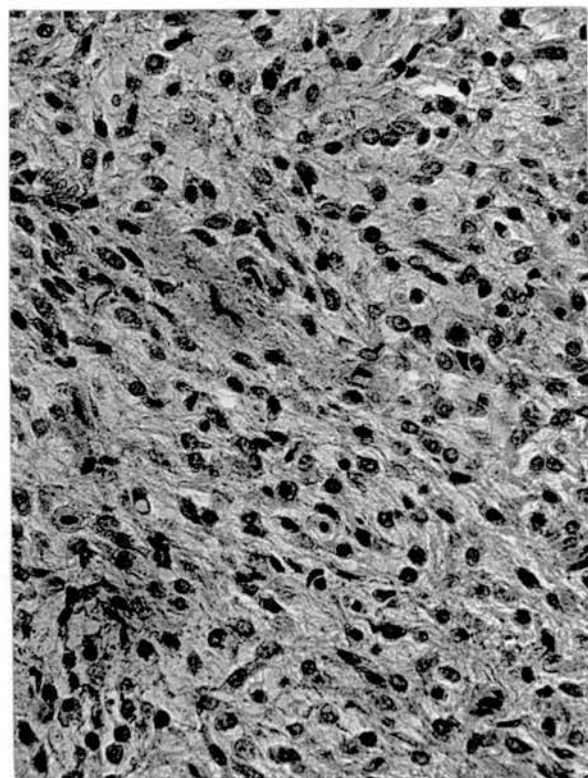


Fig. 230.

x 350.

Case 75.

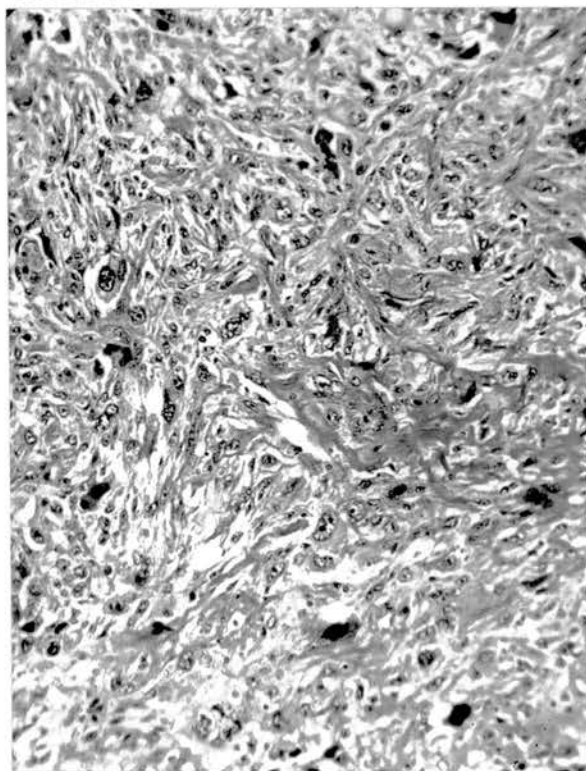


Fig 231.

x150.

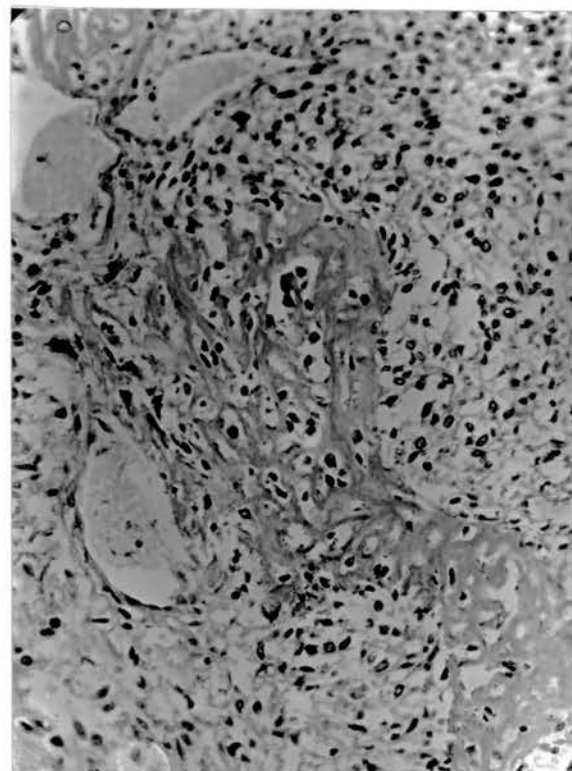


Fig. 232.

x120.

Case 76.

S.33.

History: An African farmer aged 50 complained of pain in a large tumour just lateral to the nipple, noticed for 6 months.

Examination: A soft rounded swelling was slightly movable. Aspiration removed some dark fluid and transection of the tumour showed a haemorrhagic necrotic centre surrounded by tissue which suggested sarcoma.

Histology: With the limited data and no tissue available for differential staining, diagnosis here apart from sarcoma is difficult. One area is a fibrosarcoma with some pleomorphism (fig. 233); another shows large malignant abnormal cells, some with peripheral nuclei suggestive of liposarcoma (fig. 234).

This is not a very convincing case clinically or histologically but it was sent as a mammary tumour.

Case 77.

S.145.

History: A male aged 51 noticed an enlarging mass in the breast for 3 months. It had ulcerated 3 weeks before examination.

Examination: The tumour clinically suggested a sarcoma but only local excision was done when the muscle was found invaded.

Histology: A spindle-celled fibrosarcoma with moderate mitotic activity. The pectoral muscle was invaded. There were foci of necrosis and inflammatory cell infiltration from the ulceration. The patient died later but the date was not given.

Case 76.

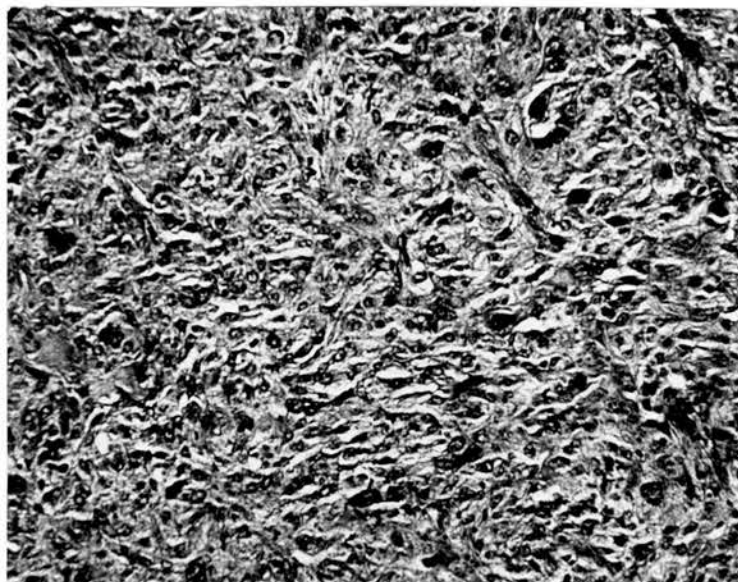


Fig. 233.

x 150.

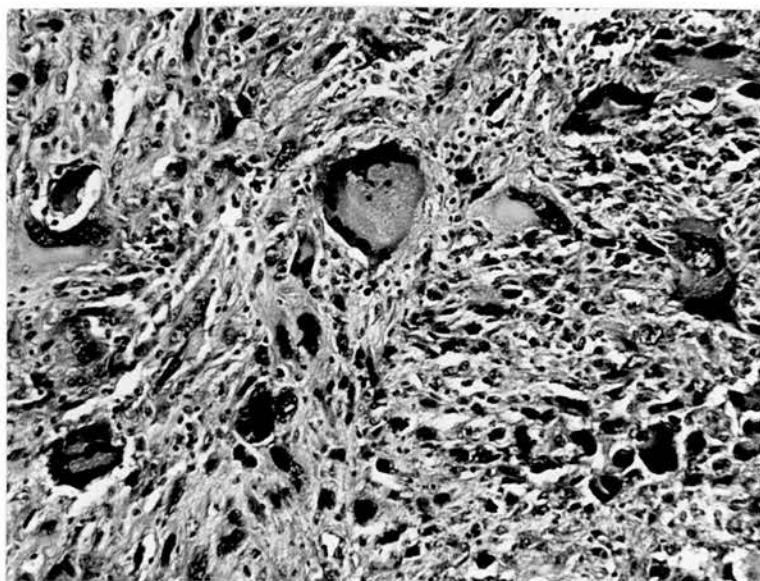


Fig. 234.

x 150.

EVOLUTION OF SARCOMA

Figs. 235 - 262.

Evolution of Sarcomas

The majority of sarcomas of the breast, with the obvious exception of such rare types as angiosarcomas and neural tumours, are developments from fibroadenomas. The demonstration of this evolution may require the examination of several areas, which is possible if the apparently benign growth is removed in toto or if the "suspicious" or malignant tumour shows some features characteristic of fibroadenomatous structure. At an advanced sarcomatous stage, no such features are usually present, but comparison with earlier tumours may then be an index to histogenesis, even when no epithelial component is present. Hertzler considered that "it has not been demonstrated that a sarcoma may develop in the breast as a primary growth", that is to say, except from a benign precursor. Fibroadenomas too small to be palpable are a frequent finding in the histological examination of mammary tissue removed for cystic hyperplasia ("chronic mastitis") and may even at that stage be very active, if not definitely sarcomatous (see figs. 235 & 236), a minute tumour only 6 mm. in its long diameter.

The many years during which the patient may have known of the presence of a tumour in the breast, from five to fifty years in cases personally examined, rules out the possibility of these growths being "malignant from the beginning", a statement which the writer finds difficult to accept for any type of tumour, human or experimental. Hieger's experimental work has emphasized the slow action of human carcinogens in general. Tumours such as nephroblastoma, retinoblastoma etc., which emerge in very early life, could be described as "malignant from the beginning" in the sense that the tissue or organ has never differentiated to normal structure, but continues to proliferate post partum at this undifferentiated level. Sarcoma, as well as carcinoma, is the end stage of a progressively atypical cell proliferation which eventually produces a malignant tissue and mammary sarcomas provide material in which this progressive evolution from benign and border-line phases can be studied. The precursor is predominantly of intracanalicular structure but occasionally also pericanalicular or of both types, as in fig. 245.

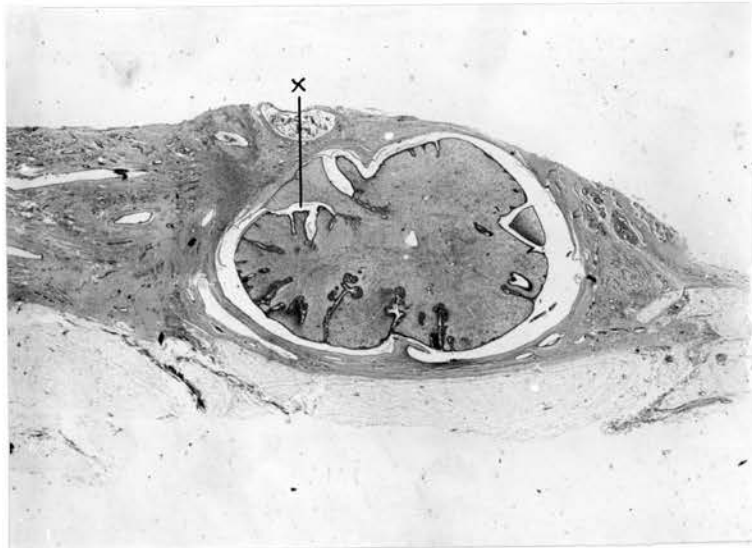


Fig. 235.

x7.

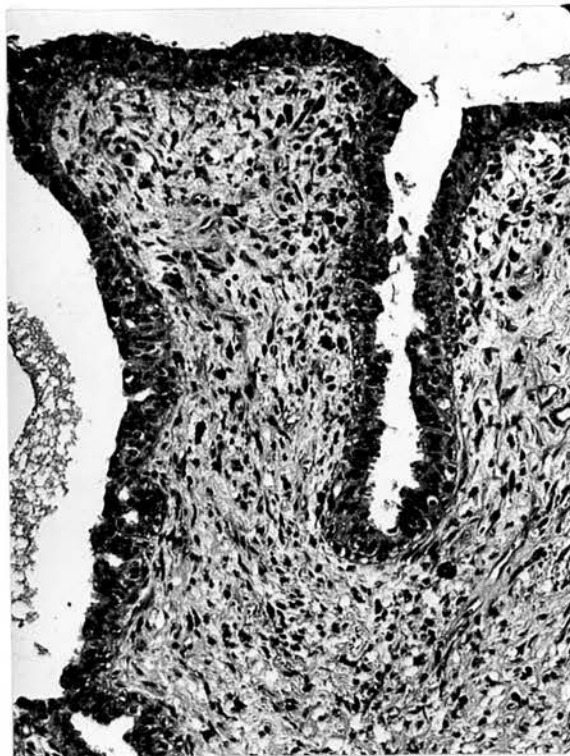


Fig. 236.

x150.

This evolution is shown briefly in the following cases:

Fig. 237. A very early fibroadenomatous structure in a single lobule. $\times 75$.

Fig. 238. Separate fibroadenomatous lobules before coalescence to form a larger tumour. $\times 50$.

Fig. 239. A large fibroadenoma, becoming mainly fibromatous, by the elimination of the epithelial component, on the right. $\times 1$.

Fig. 240. Same tumour, showing growth towards a "pure fibroma" by the compression and obliteration of the epithelium. $\times 100$.

Fig. 241. A large benign tumour, transected in the nipple plane, showing a papillary type of fibroadenoma in the upper half and almost "pure fibroma" in the lower part. $\times \frac{1}{2}$.

Fig. 242. Same tumour, transected 2 cm. lateral to the nipple plane, most of it "pure fibroma", with a little fibroadenomatous structure in the centre. $\times \frac{1}{2}$.

Fig. 243. Three benign tumours, transected in a plane lateral to the nipple, the left tumour a fibroadenoma, the right one, an almost "pure fibroma", the centre one, a mixture of both. $\times \frac{1}{2}$.

Fig. 244. The same breast, transected in the nipple plane, shows the "pure fibroma" of fig. 243 with some fibroadenomatous structure, on the left; on the right, the fibroadenoma of fig. 243 retains much the same structure. The central tumour, lying in a shallow bed in fig. 243, was detached in transecting. $\times \frac{1}{2}$.

All three benign tumours had well-defined, rather thick capsules.

Fig. 245. A large benign tumour, reaching almost to the pectoral muscle (lower right), showing both intra- and peri-canalicular structure. $\times 30$.

Fig. 246. An intracanalicular fibroadenomatous polyp containing growth of pericanalicular structure. $\times 75$.

Fig. 247. A tumour known for 12 years in a patient of 59 years, now rapidly enlarging and very vascular histologically but still considered benign. $\times 50$.

Fig. 248. A large, rather ill-defined fibroadenoma, from a patient of 38 years, with cellular stroma and occasional mitotic figures and loss of epithelium on one side of duct, but considered benign. $\times 75$.



Fig. 237.

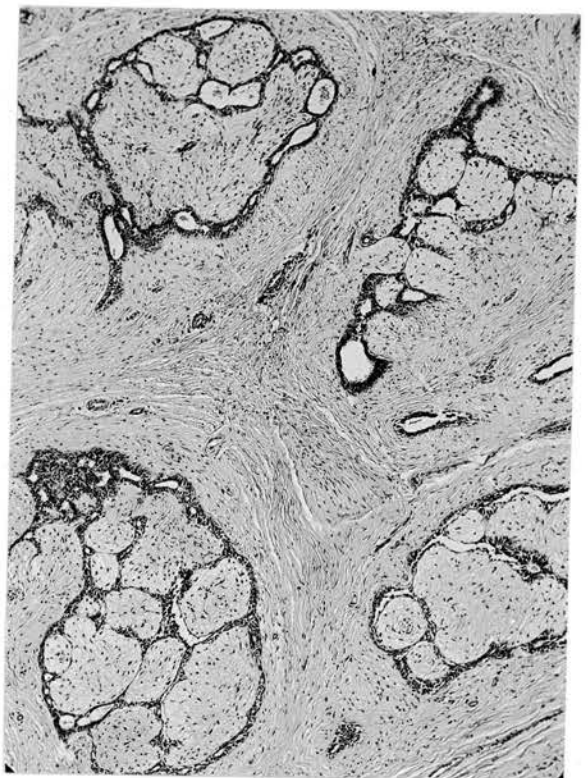


Fig. 238.

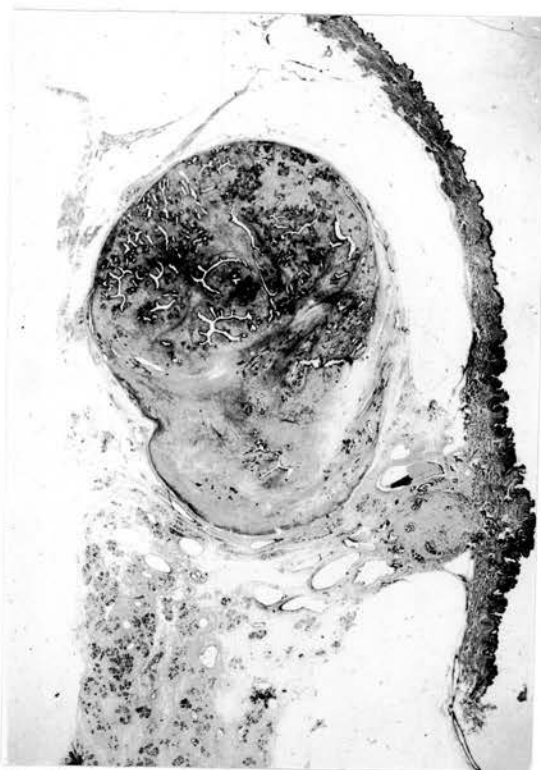


Fig. 239.

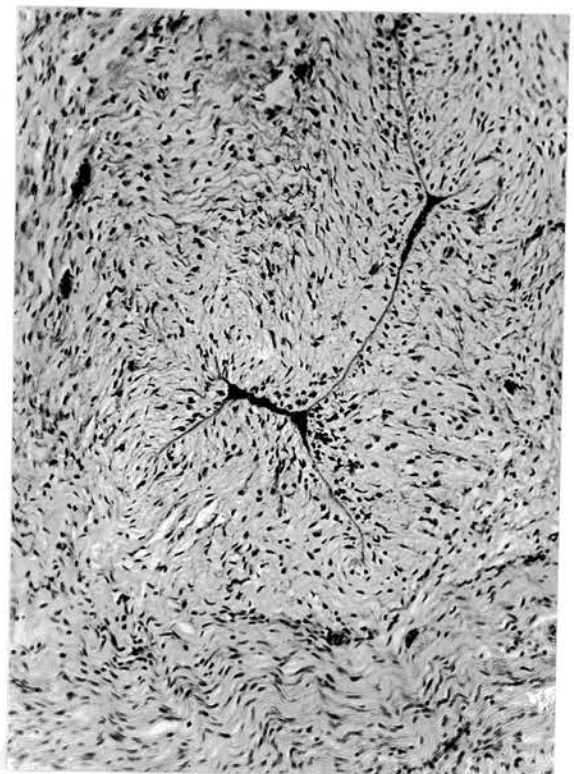


Fig. 240.

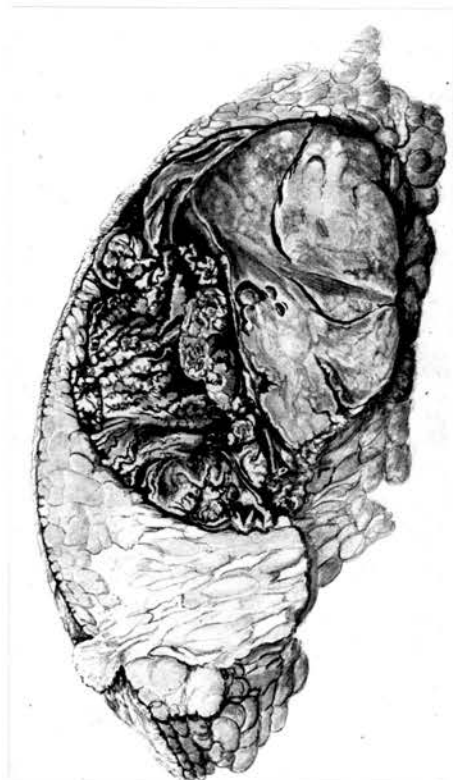


Fig. 241.



Fig. 242.

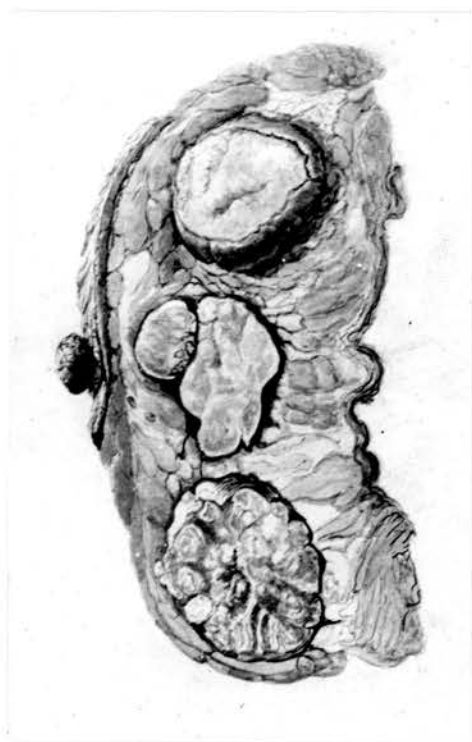


Fig. 243.

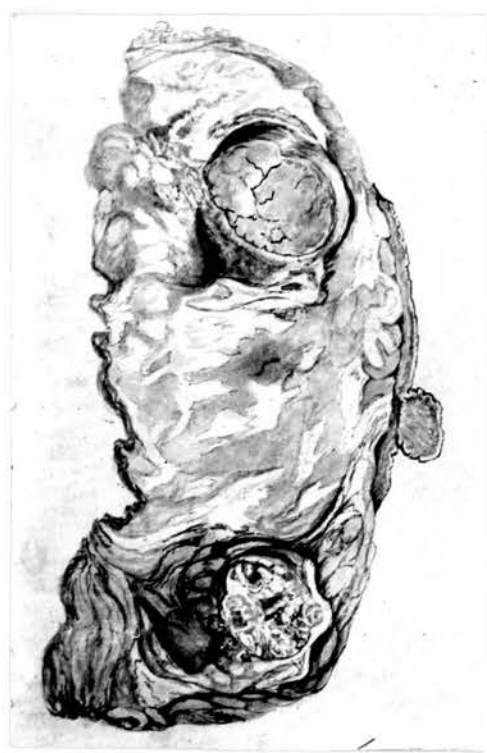


Fig. 244.

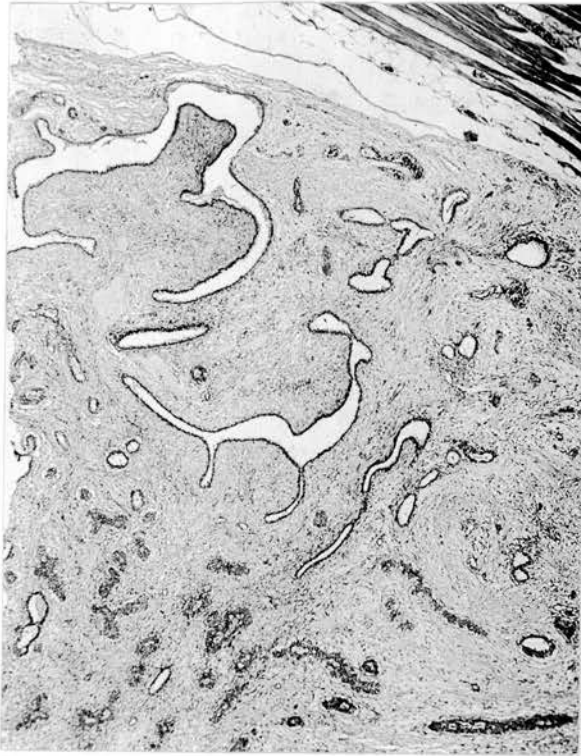


Fig. 245.

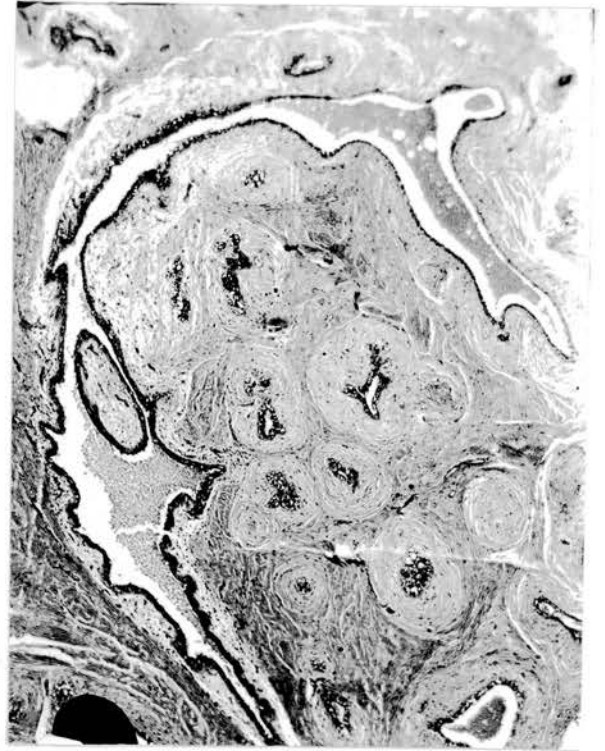


Fig 246.



Fig. 247.

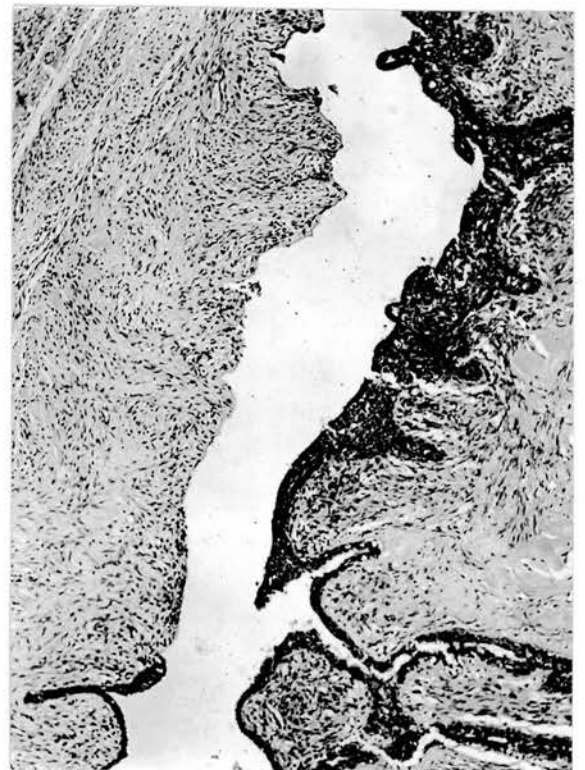


Fig. 248.

Fig. 249. A small, spherical fibroadenoma, 3 cm. in diameter, which shelled out easily, showing active periductal stroma with some mitotic figures but considered benign. $\times 55$.

Fig. 250. The same tumour, with early merging of active stroma and early mucin formation, upper left. A benign tumour, but apparently progressive. $\times 100$.

Fig. 251. Part of a large fibroadenoma, with numerous mitotic figures, a "border-line" picture, if not early malignancy. $\times 150$.

Fig. 252. A large fibroadenoma, which at low power magnification, does not look suspiciously active. $\times 30$.

Fig. 253. Same tumour, but definitely malignant, with 15 mitotic figures in this field. It suggests differentiation to unstriped muscle, with the long spindle cells and some palisading but no differential stains available. $\times 150$. The low power field is certainly fibroadenomatous.

Fig. 254. A well-defined intracanalicular fibroadenoma, with a broad capsule, but scattered large atypical nuclei in the active stroma, especially lower right. $\times 20$.

Fig. 255. Same tumour area. $\times 50$.

Fig. 256. Same tumour, showing the large, irregular nuclei, more obvious in this polypoid formation. $\times 150$. This tumour recurred as a fungating mass, in the operation scar, but this tissue was not sent for examination.

Fig. 257. A cystic fibrosarcoma, partly spindle-celled, partly, as here, of "cauliflower" type, with atypical, larger nuclei in the polypoid outgrowths. There was much epithelial desquamation. $\times 20$.

Fig. 258. A malignant fibroadenoma, with a duct embedded in myxosarcomatous tissue, and some pleomorphism. $\times 140$.

Fig. 259. A similar myxosarcoma, with many branching atypical nuclei. $\times 220$.

Many mammary sarcomas show varying stages of this myxomatous change, and it may appear as a recurrence of a spindle-celled fibrosarcoma, as in case 15 fig. 69. It indicates not a stromal degeneration but an enhanced malignancy.

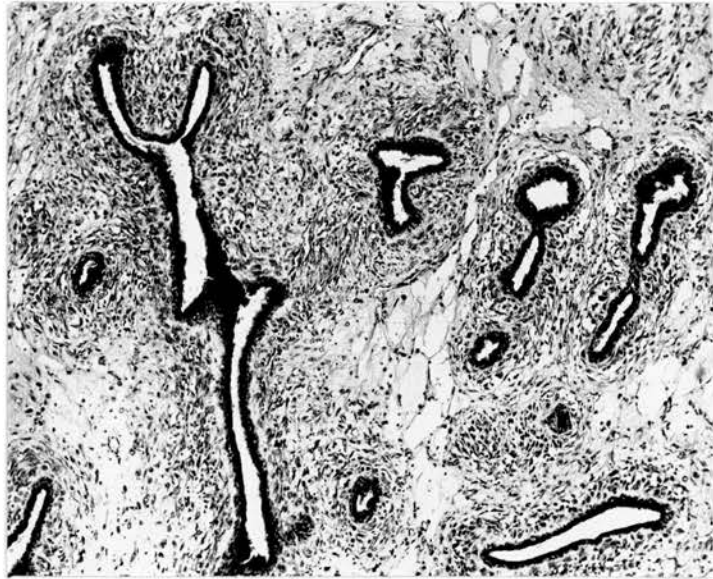


Fig. 249.

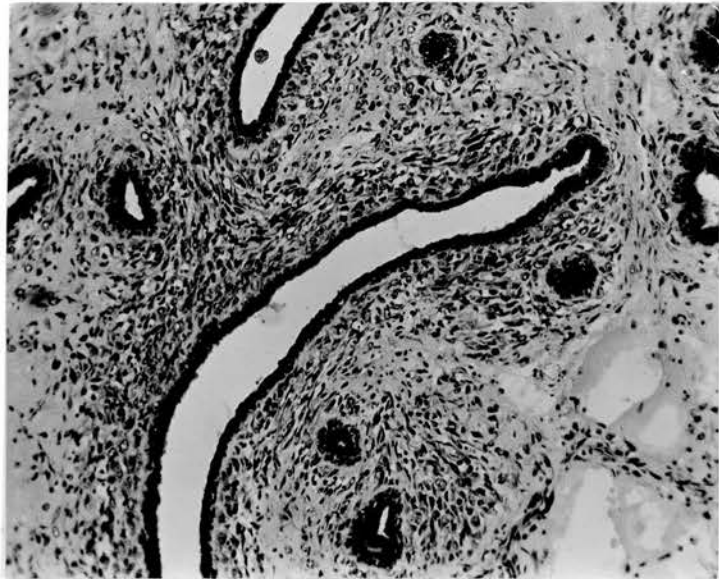


Fig. 250.

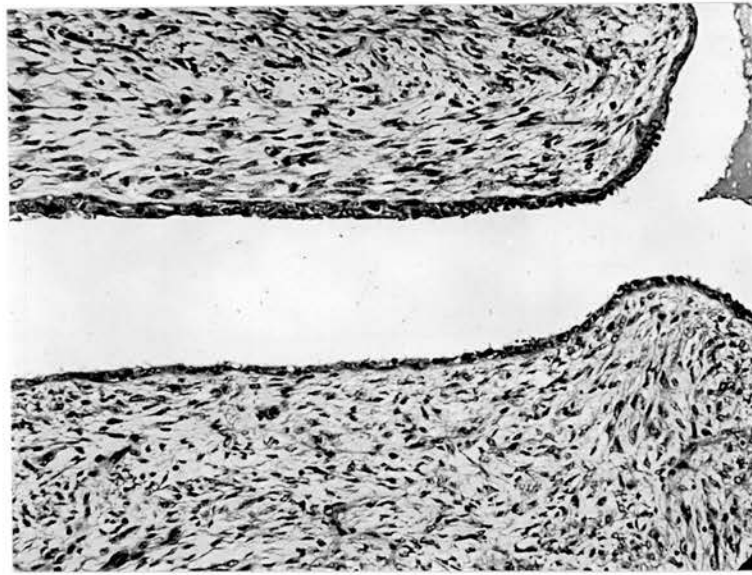


Fig. 251.

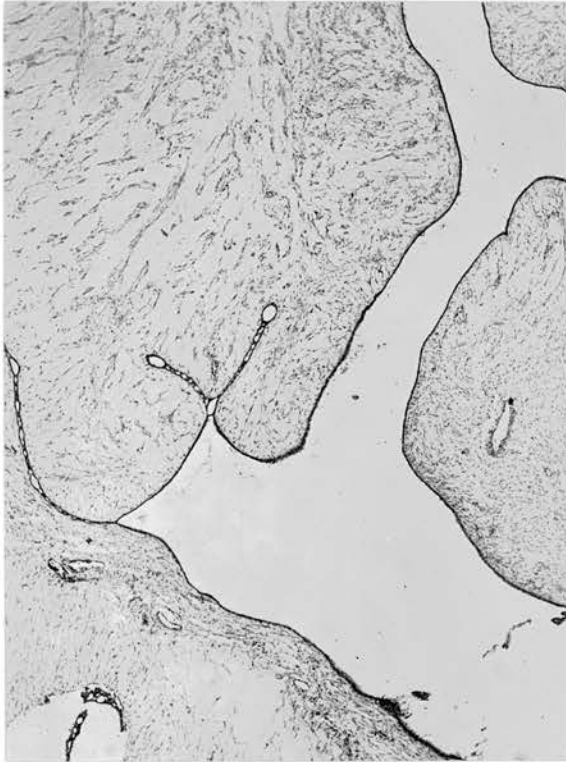


Fig. 252.

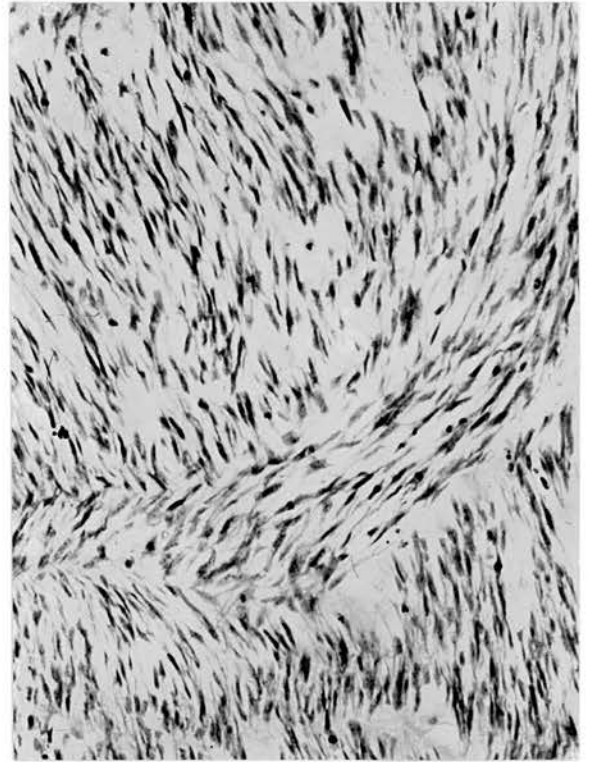


Fig. 253.



Fig. 254.

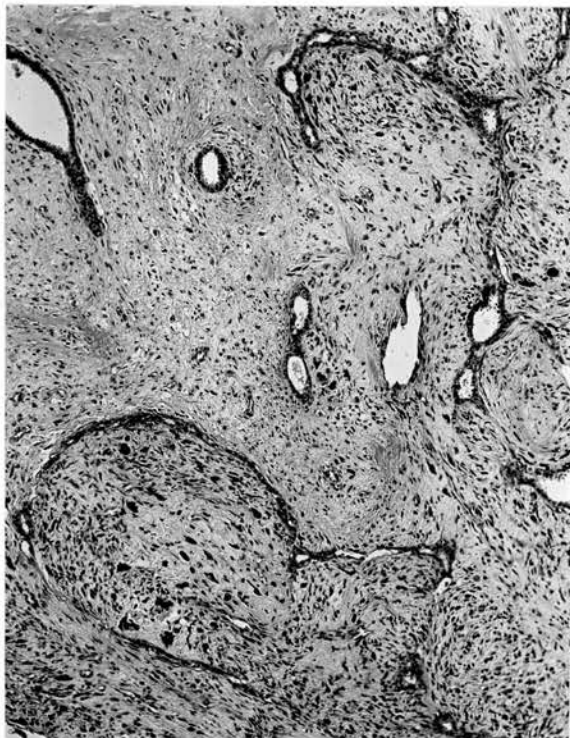


Fig. 255.

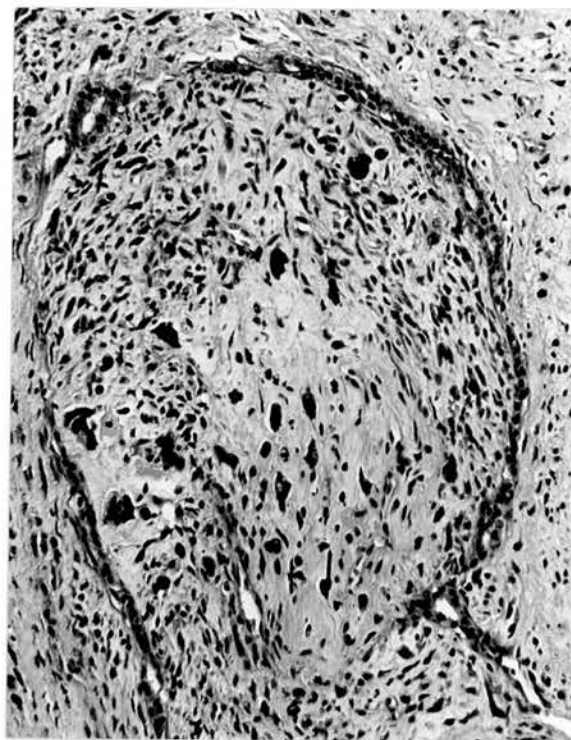


Fig. 256.

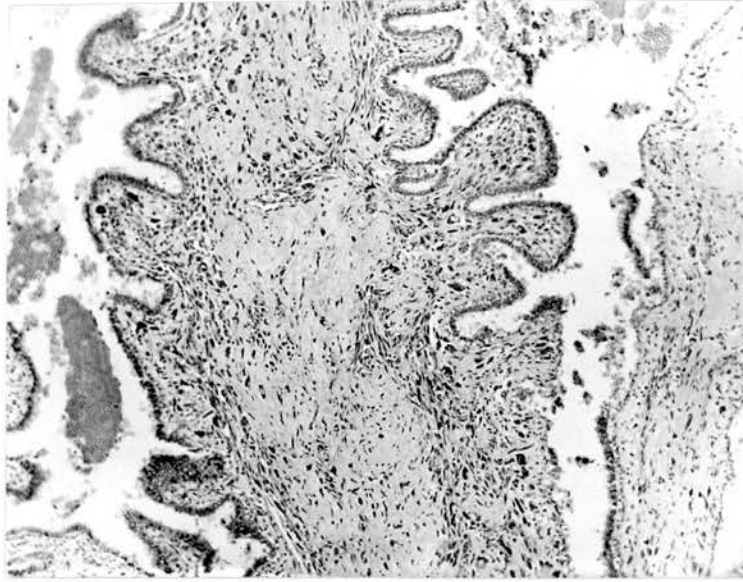


Fig. 257.

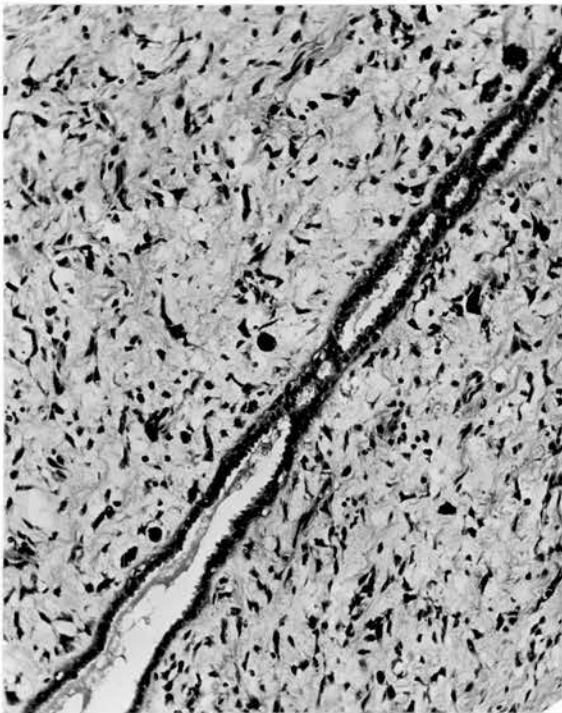


Fig. 258.



Fig. 259.

Fig. 260. An intracanalicular fibroadenoma, with mildly active but benign stroma. x 50.

Fig. 261. A "suspicious" picture, with the scattered large atypical nuclei illustrated also in figs. 254 - 256.

Fig. 262. This tumour is a fibrosarcoma, with many mitotic figures but little pleomorphism. x 400.

These last three separate fibroadenomatous growths were in fairly close approximation in the same breast of a patient of 46 years. They underline the necessity of adequate removal of tumour tissue in middle-aged and older patients.

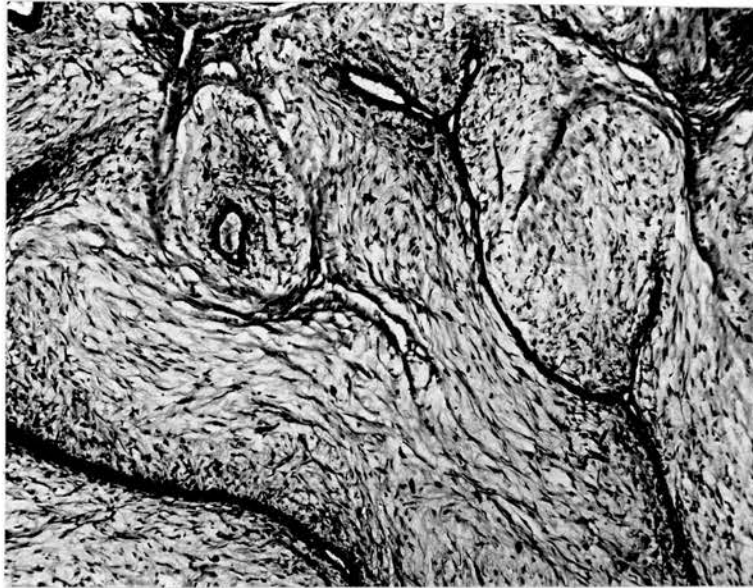


Fig. 260.



Fig. 261.

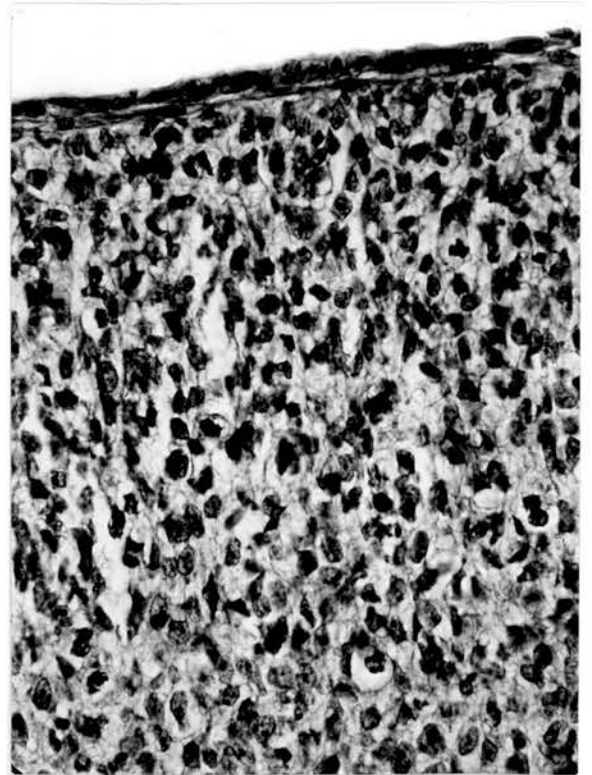


Fig. 262.

CARCINOMATOUS FIBROADENOMA

Cases 78 - 86. Figs. 263 - 285.

Carcinomatous fibroadenoma

Unless at a very advanced stage of growth when all epithelial elements may have been obliterated, some trace of a fibroadenomatous histogenesis is usually detectable in many, if not the majority of sarcomas of the breast, if adequate tissue is examined. The obvious exceptions are the rare haemangiosarcomas and the even rarer neural tumours.

Progressive activity in a fibroadenoma may produce malignant growth in the epithelial component, a carcinomatous fibroadenoma. This is a much rarer development than adenofibrosarcoma or "pure sarcoma" and there are few references to it in the literature (Fox 1934, Tudhope 1939, Foot 1943, Harvey Smith 1949, Stout 1954).

Among the several hundred fibroadenomas examined personally, the epithelial tissue has shown carcinomatous change in at least 9 cases. These carcinomatous fibroadenomas are illustrated here with brief notes. The pattern they show is rather surprisingly uniform. (1) The tumour is initially a cystic intracanalicular fibroadenoma, with the exception of the first and sixth cases. (2) The multi-layered epithelium is squamoid or squamous (a finding also by Sandison). (3) The polypoid stromal masses show considerable proliferative activity but rarely of definitely neoplastic type, with the exception of the fifth case. In the first and ninth cases, in contrast, the stroma of the tumour is quiescent and hyalinized.

Sarcomas of the breast very rarely extend to axillary lymph nodes, even in large and advanced tumours. Increased vascularity, evident as the proliferation of blood capillaries, is the usual indication of progressive activity towards malignant mesenchymal growth, but I have been unable to trace any associated lymph vessel proliferation within a mammary sarcomatous tissue. The characteristic expansile growth of sarcomas also appears to compress or obliterate the lymph channels surrounding the tumour and thus to explain the extreme rarity of axillary lymph node involvement. A blood-borne invasion via the hilar vessels would be possible in metastatic dissemination into lymph nodes. With carcinomatous development in a fibroadenoma, lymph nodes may be invaded, as seen in two of the cases of carcinomatous fibroadenoma described and possibly also in a third where there was peripheral invasion of lymph vessels but no node tissue available for examination.

Carcinomatous Fibroadenoma

| Series | Reference | Age | Duration of tumour. (years). | Type | Nodes | Therapy | Outcome in years. | Metastases |
|--------|-----------|-----|------------------------------------|--------------------------------|-------|--------------------|---------------------------------------------------------|------------|
| 78 | 382 | 47 | ? | Carcinomatous fibroadenoma. | - | Local excision | Carc.other breast. | - |
| 79 | 579 | 28 | 6/52 | do. | - | Local excision | Alive 5. | - |
| 80 | 1847 | 76 | ? | do. | - | ? | ? | - |
| 81 | 814 | ? | ? | do. | - | ? | ? | - |
| 82 | S.145 | 40 | 3/12 | do. | - | Radical mastectomy | Recurrence cervical node Died 4 ² /12. | - |
| 83 | S.118 | 45 | 8/52 | do. | - | Local excision | Recurrence 8/12 Died ? | - |
| 84 | 506 | ? | ? | do. | - | ? | ? | - |
| 85 | 553 | 52 | ? | do. | + | Radical mastectomy | ? | - |
| 86 | 325 | ? | ? | do. | + | Radical mastectomy | ? | - |

Case 73.

392.

History: The patient, aged 47 years, had a local excision for this clinical fibroadenoma. At the same time, she had a radical mastectomy for a carcinoma of the other breast which infiltrated the skin and pectoralis major and had metastasized to several axillary lymph nodes. This was a Canadian patient and no further data were available.

Histology: There is no carcinoma in the breast beyond the defined periphery of the fibroadenoma but some tissue infiltration is shown within the tumour (fig. 263). Another area of the fibroadenoma shows more intraductal carcinoma (fig. 264) and the third area, at higher power, the squamoid hyperchromatic cell type with mitotic figures (fig. 265). The very quiescent stroma in all fields is noteworthy. The pathologist emphasized the fact that there was no possibility of extension into the tumour from any adjacent carcinoma in the breast.

Case 79.

579.

History: The patient aged 28 years noticed a lump in the breast for 6 weeks, increasing in size.

Examination: No other lumps in either breast, no palpable nodes and no evidence of tumour elsewhere were found. Last child 3 years old. The surgeon was reluctant to do a mastectomy because of her young age. Local excision done with release of blood-stained fluid on transection. Patient seen regularly since operation and alive and well exactly 5 years later.

Histology: An intracanalicular fibroadenoma in a cystic tissue with both components showing active growth. The epithelium is many-layered, squamoid in type and malignant with considerable mitotic activity and early infiltration. The stroma is also proliferative but not neoplastic (fig. 266).

Case 80.

1847/37.

History: No data are available of this case except the age of the patient, 76 years, with a cystic tumour.

Histology: Polypoid masses of moderately active fibrous tissue, covered by irregular, many-layered bands of squamoid epithelium with scattered mitotic figures and very early invasion (fig. 267).

Case 81.

814.

History: An old specimen cut as a whole breast section. The only clinical description available was a very large cystic tumour possibly "Brodie's tumour" or "Cystosarcoma phyllodes".

Histology: Polypoid stromal masses are covered by pleomorphic squamous carcinoma (fig. 268) which shows invasive downgrowth at several points into the active fibroblastic stroma (Right edge of fig. 268). Fig. 269 shows the proliferation of both components with pleomorphic epithelial cell invasion with mitotic figures but the stroma is not considered neoplastic.

Case 78.



Fig. 263.

x60.

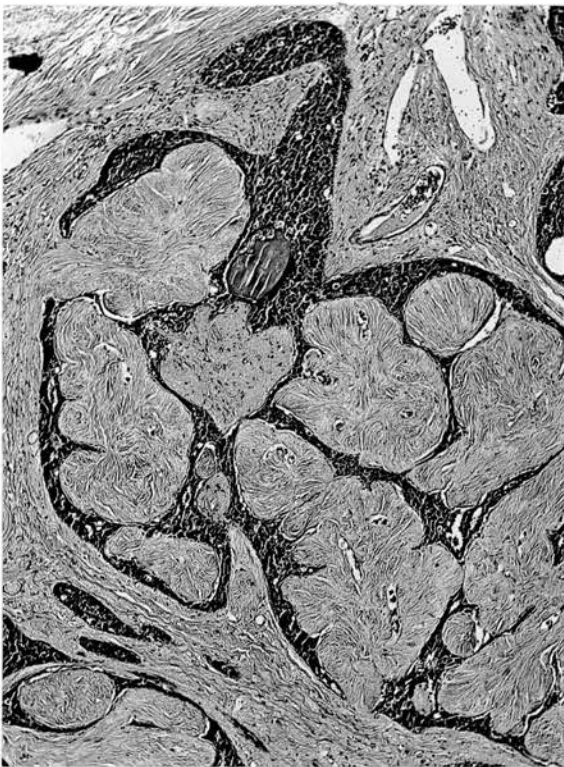


Fig. 264.

x60

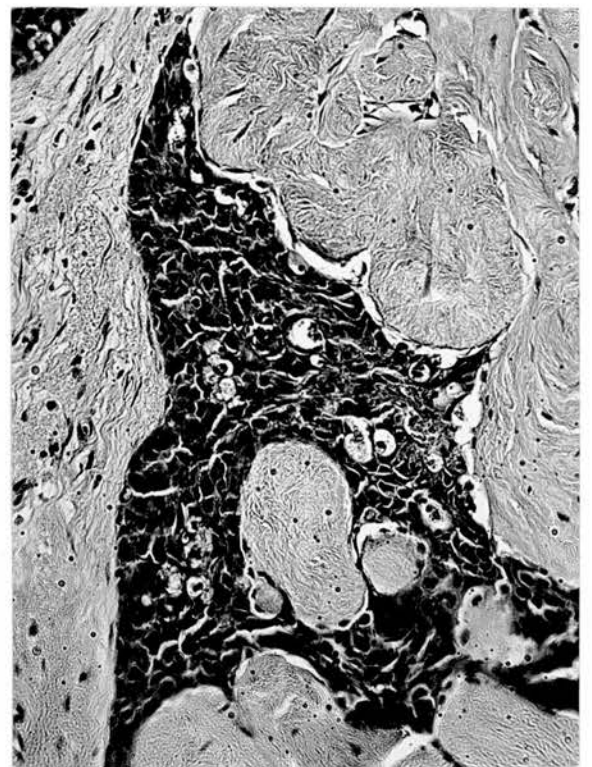


Fig. 265.

x225.

Case 79.

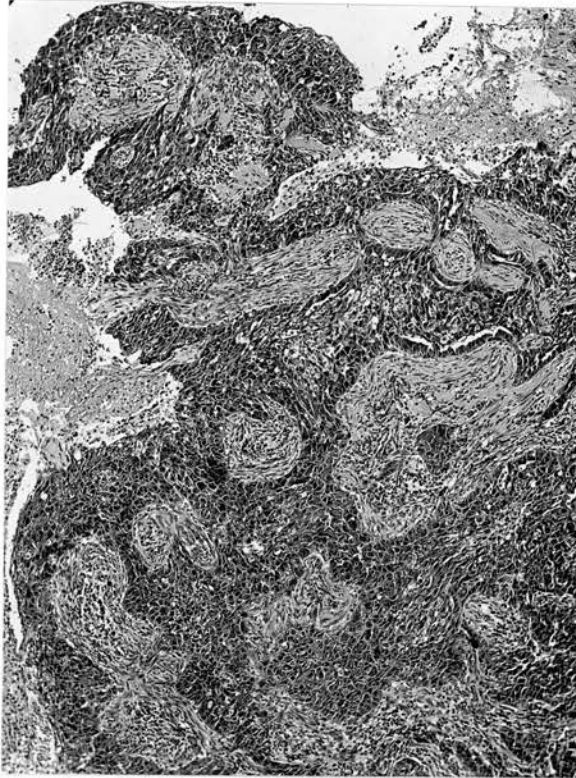


Fig. 266

x50.

Case 80.



Fig. 267.

x50.

Case 81.

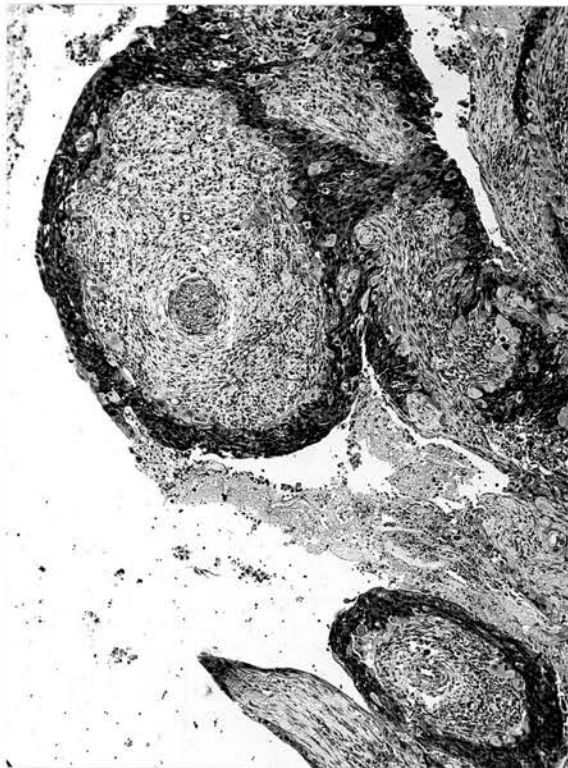


Fig. 268

x60.

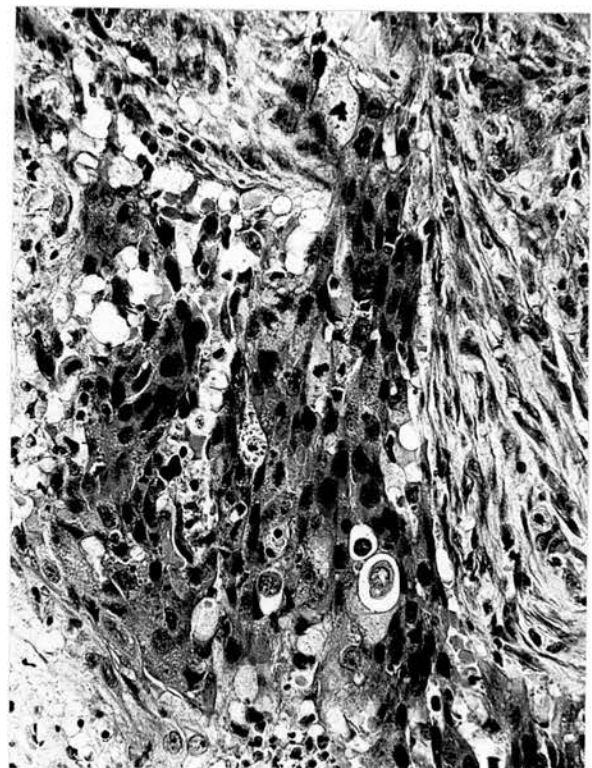


Fig. 269.

x250.

Case 82.

S.145.

History: The patient, a diabetic, aged 40 years noticed a lump in the breast for 3 months, tender and increasing in size.

Examination showed a huge fatty breast with a tumour in the axillary tail, which suggested origin as a papilloma or a fibroadenoma. There were enlarged soft nodes in the axilla. Radical operation was done.

Histology: Polypoidal masses of stroma are covered by many-layered bands of malignant squamous epithelium which at low power magnification shows no obvious downgrowth (fig. 270, H & E section), but extensive detachment from the underlying stroma. This stroma is highly pleomorphic, with bizarre giant cells, many mitotic figures (figs. 271 & 272) and suggestive of some lipomatous metaplasia. In one or two areas, defined masses of the covering malignant epithelium show invasion into this atypical stroma (fig. 273). Four axillary nodes examined were negative.

Later, on readmission to control the diabetes, an enlarged cervical node was found and excised. It showed squamous carcinoma. She died 2 months later, a post-operative survival of 4 years 2 months.

This could be diagnosed as a carcinosarcoma but the relation of the component tissues points to histogenesis as a fibroadenoma in which epithelium and stroma have both become malignant. It may be that some carcinosarcomas of the breast arise in this way. Carcinomatous fibroadenoma and carcinosarcoma are certainly both very rare types of mammary tumour.

Case 82.



Fig. 270.

x 30.



Fig. 271.

x 50.

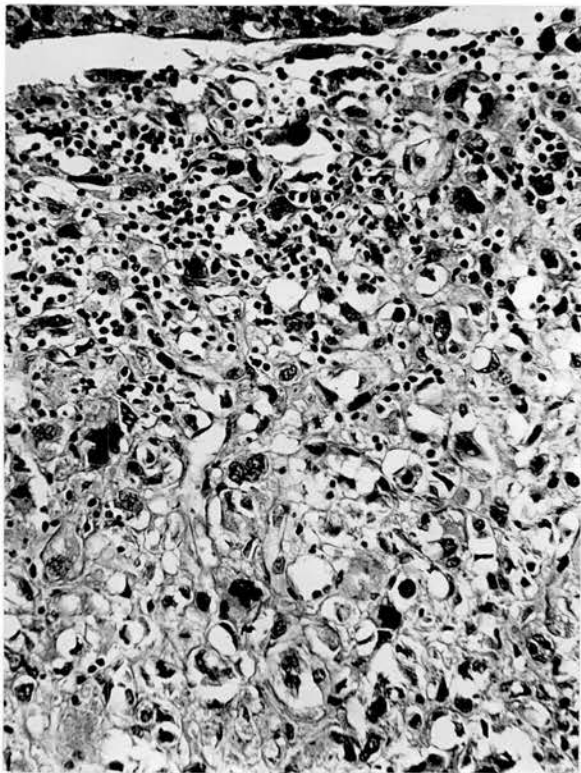


Fig. 272.

x 250.

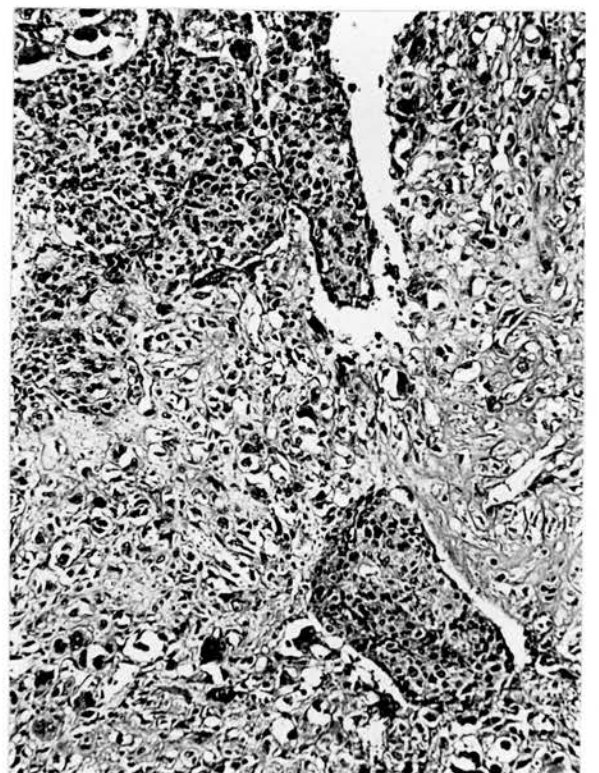


Fig. 273

x 100.

Case 83.

S.118.

History: The patient, aged 45 years, had noticed the tumour for only 8 weeks. She was very emaciated.

Examination showed a massive breast with an ulcerated fungating growth. It was excised and 8 months later she was readmitted with a massive recurrence 10 cm. in diameter in the operation area but without other signs of disease. The tumour tissue was removed piece meal and was white and fibrous, looking more like sarcoma than the primary growth.

Histology: The primary tumour showed areas of irregular fibroadenomatous structure with many-layered covering squamous carcinoma already invading the active stroma (fig. 274). There was much squamous carcinoma beyond the fibroadenomatous part (fig. 275), much of it of highly anaplastic type with prickle-cell formation (fig. 276). The recurrent growth showed scattered monstrous multinucleated cells in a predominantly spindle-cell tissue, which is regarded as a possible spindle-cell carcinoma (fig. 277). She died at home, date uncertain. There was no autopsy.

This is a very unusual and obviously very advanced malignant condition.

Case 83.

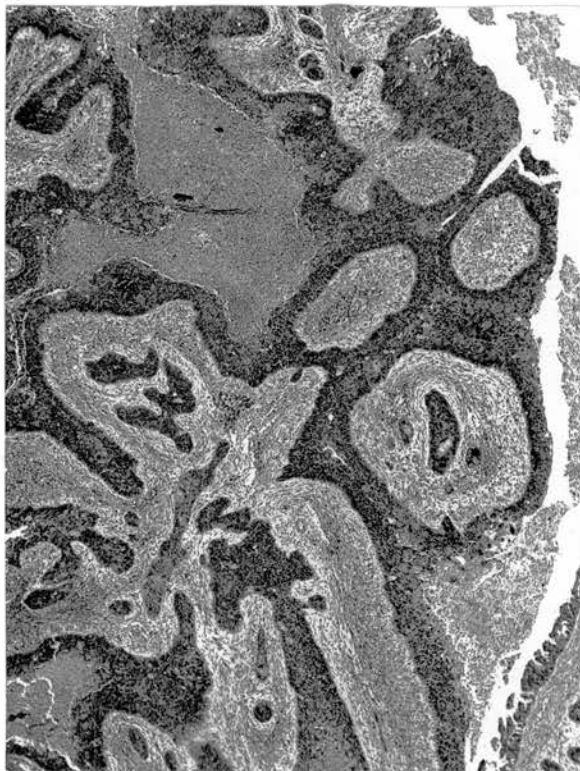


Fig. 274.

x35

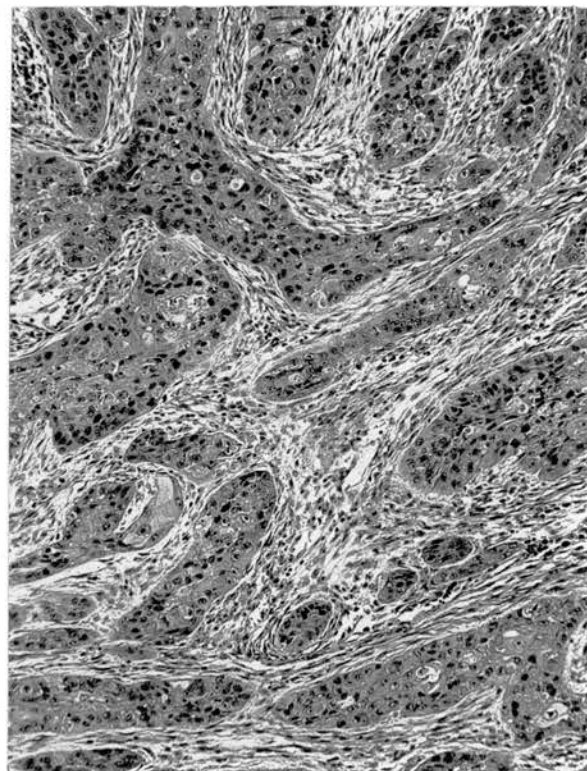


Fig. 275.

x100.

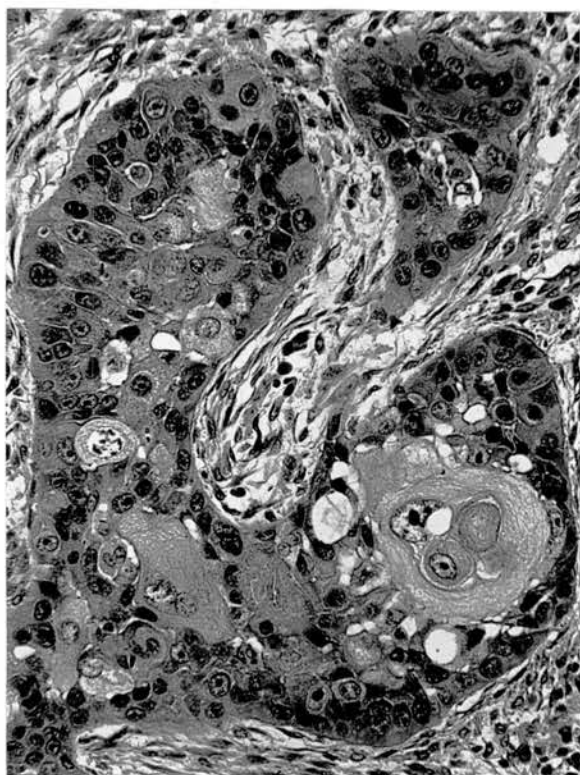


Fig. 276

x275

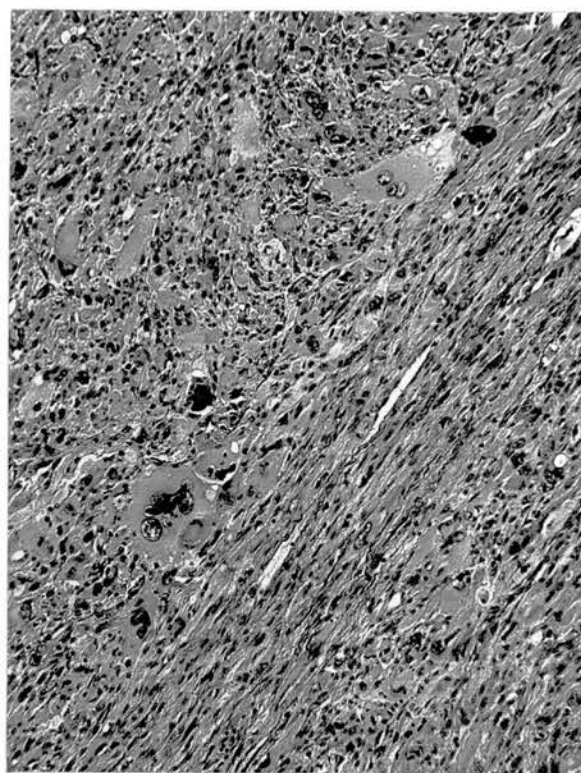


Fig. 277.

x100.

Case 84.

506.

History: This was sent as an unusual mammary tumour but without data.

Histology: A fibroadenomatous structure with irregularly multilayered epithelium suggestive of downgrowth into the polypoid stromal masses (fig. 278). A small part of a duct is seen at the upper edge (fig. 279) with deeper discrete carcinomatous deposits in a mildly fibroblastic background. There is much carcinomatous infiltration near the periphery of the tumour, of similar squamoid type and some of it appeared to be in lymph vessels.

Case 85.

553.

History: The patient was aged 52 years but no clinical data were given.

Histology: A fibroadenomatous structure, with many-layered malignant squamous epithelium covering the active stromal polyps. The epithelium shows some pleomorphism with mitotic activity and obvious infiltrative downgrowth (fig. 280). The lymph node is invaded with strands and small plaques of carcinoma (fig. 281).

Case 84.

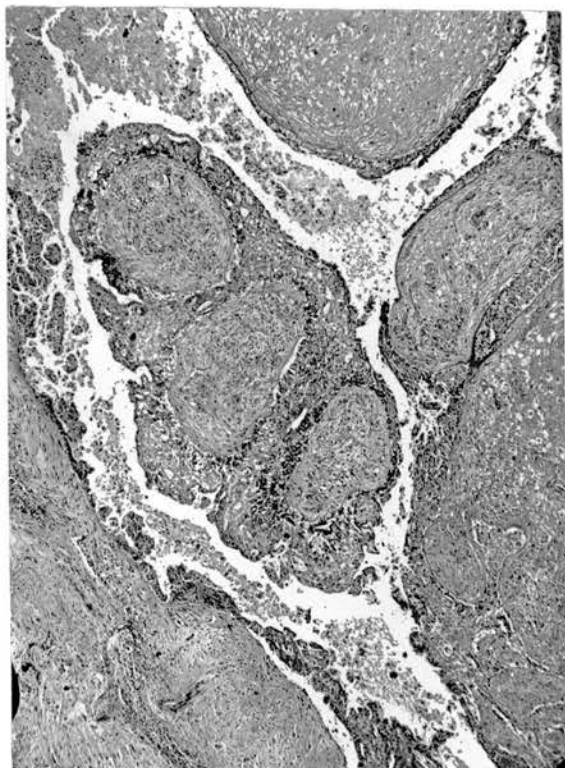


Fig. 278

x35

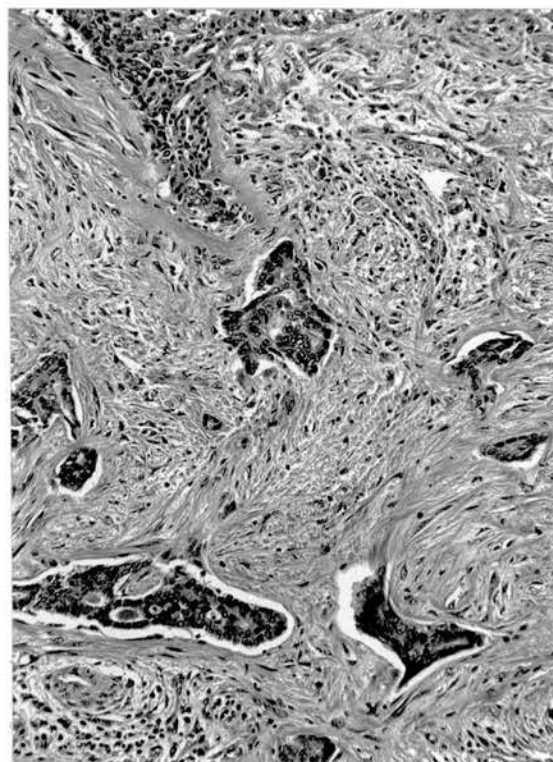


Fig. 279.

x100.

Case 85



Fig. 280

x 50

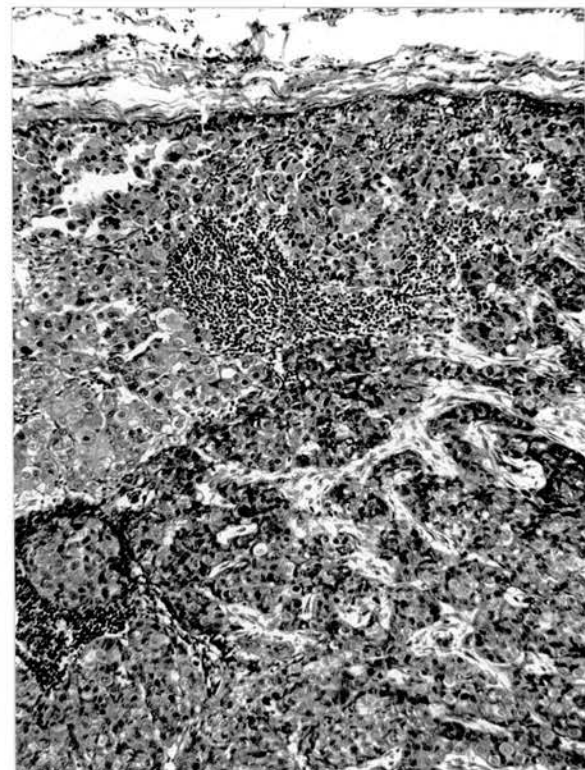


Fig. 281.

x100.

Case 86.

325.

History: No data are available in this case except the presence of a defined, mobile mammary tumour, with palpable axillary nodes.

Histology: Fibroadenomatous structure with dilated ducts is apparent in most of the area (fig. 282). Much of the periphery is defined but with no definite capsule and the corpus mammae beyond it shows only a few scattered ducts. A polypoid outgrowth lined by malignant squamoid desquamating epithelium is formed of hyalinised stroma with very little vascularity (fig. 283). Two axillary nodes are invaded by carcinoma (fig. 284). They show some fibrosis and a diffuse infiltration by squamoid carcinoma with little if any glandular structure (fig. 285).

The quiescent stroma of this tumour and the lymph node picture suggest a long-standing neoplasm.

Case 86.

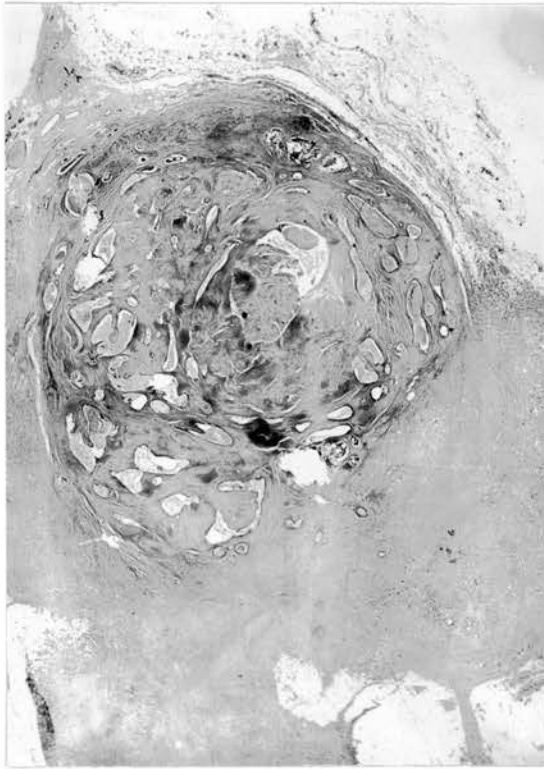


Fig. 282

x3.



Fig. 283

x50.

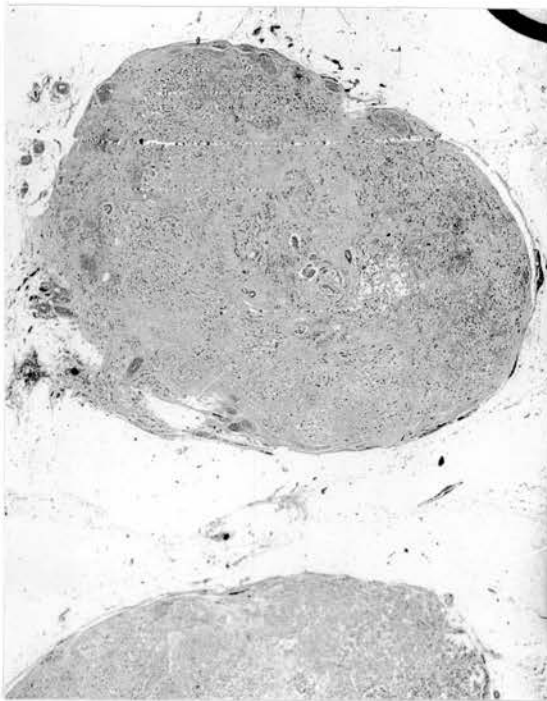


Fig. 284.

x4.

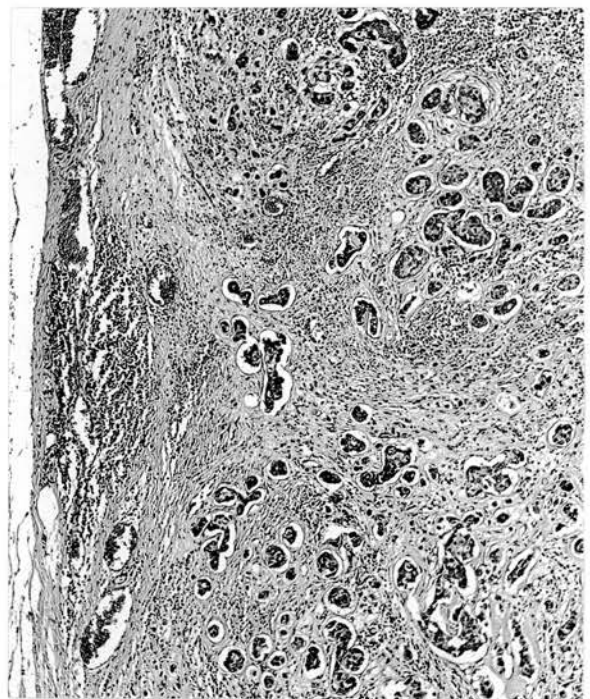


Fig. 285

x50.

CARCINO-SARCOMA

Cases 87 - 94. Figs. 296 - 310.

Carcinosarcoma

Earlier pathologists were unwilling to accept the concept of a combined tumour carcinosarcoma. In his earlier works, Willis (1934) regarded the term carcinosarcoma as having no justification, attributing the appearance to the capacity of carcinomas to assume a structure of purely sarcomatous appearance. More recent workers however have accepted the tumour although it is still a subject of debate and the diagnosis demands rigid criteria. Thus Saphir & Vass (1938), reviewing 153 reported cases, accepted only 3 or 4 of these as possibly true examples. Apparently none of the 29 mammary cases they reviewed ^{was} ~~were~~ acceptable. Their arguments against true carcinosarcoma stressed (a) the varied morphology of carcinoma cells, especially when they assume spindle shapes and are interpreted as spindle-cell sarcoma, an error particularly associated with squamous cell carcinoma (cf. Figs. 335 - 337 and 338 - 340); (b) a chronic inflammatory condition producing much fibrous tissue and regarded as part of the malignant stroma of a carcinoma; (c) the invasion of a cellular but benign connective tissue tumour by carcinoma and (d) the invasion of a sarcoma ^{by} ~~into~~ normal or hyperplastic epithelial elements. It is obvious from these restrictions that a possible carcinosarcoma needs much critical examination.

Meyer divides carcinosarcomas into 3 groups, "collision", "combination" and "composition". "Collision" implies the mingling of two independent malignant growths; "combination" tumours are those derived from a common, undifferentiated cell ancestor, as in the Wilms tumour and the "composition" type is a tumour formed by the localised malignant transformation of both parenchyma and stroma. It is clear that the recognition of these varying types demands the examination of much tumour tissue in any individual case.

Carcinosarcomas have been described in many organs of the body but are most frequently encountered in the uterus and breast, as was pointed out in the paper by Saphir and Vass.

The cases described as carcinosarcoma in this study have been critically examined and are considered as valid examples. Differential staining has been employed as a necessity in most of these especially to show the disposition of reticulin; further confirmation is given by metaplasia of the malignant mesenchymal element to cartilage

formation (Fig. 287) or fat (Figs. 271 - 273).

A carcinosarcoma is occasionally derived from a fibroadenoma which in itself is a benign "mixed" tumour with both components capable of neoplastic proliferation.

Carcinosarcoma

| Series | Reference | Age | Duration of tumour (years). | Type | Nodes | Therapy | Outcome in years. | Metastases |
|--------|-----------|-----|--------------------------------------|----------------|-------|--------------------------------------|-----------------------------|------------|
| 87. | S. 174 | 56 | ? | Carcinosarcoma | + ca. | Simple mastectomy | ? | - |
| 88. | 1324 | 69 | 3/52 | do. | - | Simple mastectomy | Alive 1. | - |
| 89. | S. 151. | 52 | 2/12 | do. | - | Radical mastectomy after delay. | Died 2 ⁶ /12. | Brain |
| 90. | 1215. | 37 | 1/12 | do. | - | Radical mastectomy + irradiation. | Alive 5. | - |
| 91. | S. 144. | 38 | ? | do. | - | Irradiation + hormones. | Alive 19. | - |

For Comparison.

| | | | | | | | | |
|-----|----------------|------------|---|-----------------------------------|---|--------------|-----------------------------------|---|
| 92. | 694. | 64 | ? | Carcinosarcoma uterine cervix. | - | Hysterectomy | Recurrence 2 ⁶ /12. | - |
| 93. | R.C.S. 219 | Male 75 | ? | Carcinosarcoma of kidney. | - | Nephrectomy | Recurrence Rapidly fatal. | - |
| 94. | R.C.S. 338. | 69 | ? | Carcinosarcoma of stomach. | + | Gastrectomy | Died | - |

Case 37.

S.174.

History: The patient aged 56 had a large lump in the breast attached to the skin.

Examination: A needle biopsy showed a fibromatous or fibrosarcomatous tumour but no carcinoma. Simple mastectomy showed a large tumour 6.3 x 5.5 x 4.5 cm. in the upper outer quadrant about 2 cm. from the nipple. It was fairly soft, grey and gelatinous, haemorrhagic in parts with a fairly well circumscribed periphery. In contact and apparently continuous with its inferior pole was an irregular mass about 3 cm. in diameter of obvious carcinoma (fig. 286).

Histology: This is a carcinosarcoma. The sarcomatous area shows many foci of cartilage of different size arising in a cellular fibroblastic matrix (fig. 287). The carcinoma is both intraductal and infiltrating (fig. 289) and is growing in and outside the sarcomatous area. The epithelial and mesenchymal components are seen in the same field in fig. 288. The carcinoma alone invaded the axillary nodes (fig. 290). No later note is available.

Case 87.

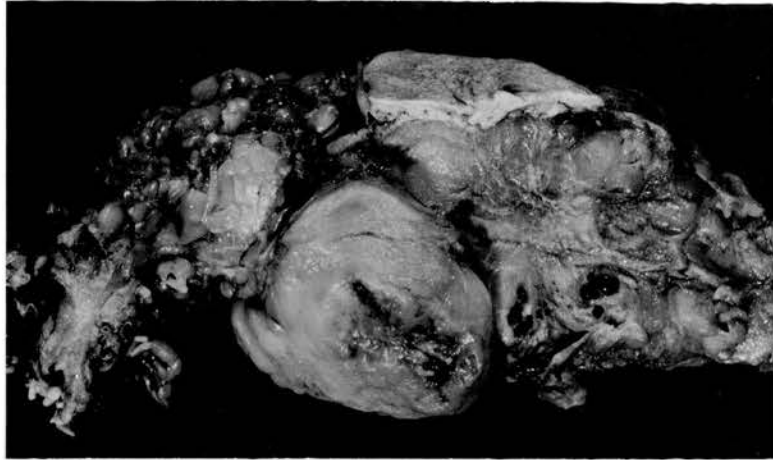


Fig. 286

x 1.

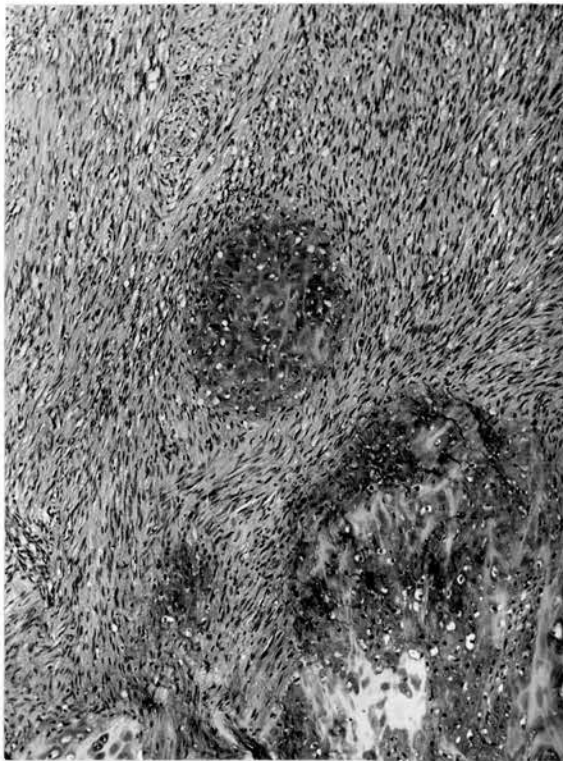


Fig. 287.

x 60.

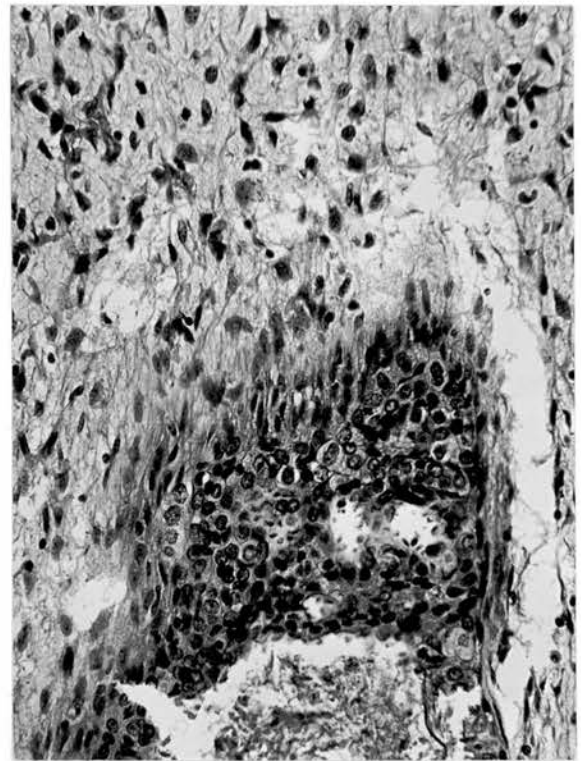


Fig. 288

x 250.

Case 87.

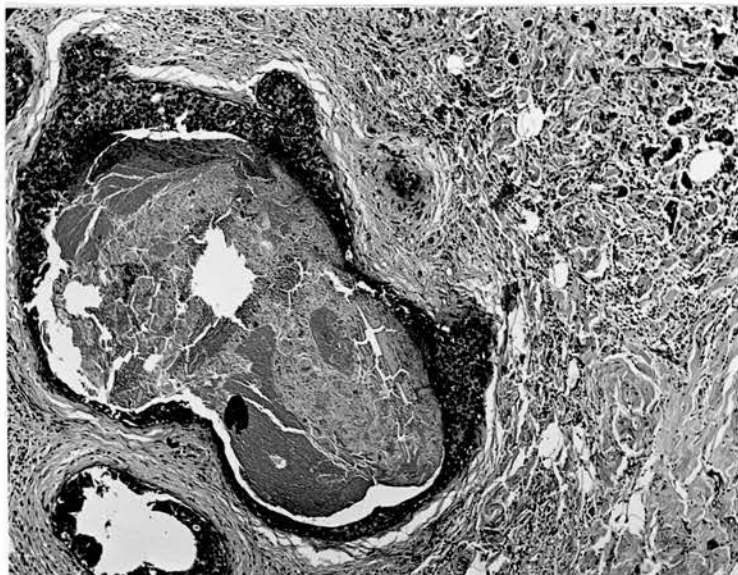


Fig. 289.

x 60.

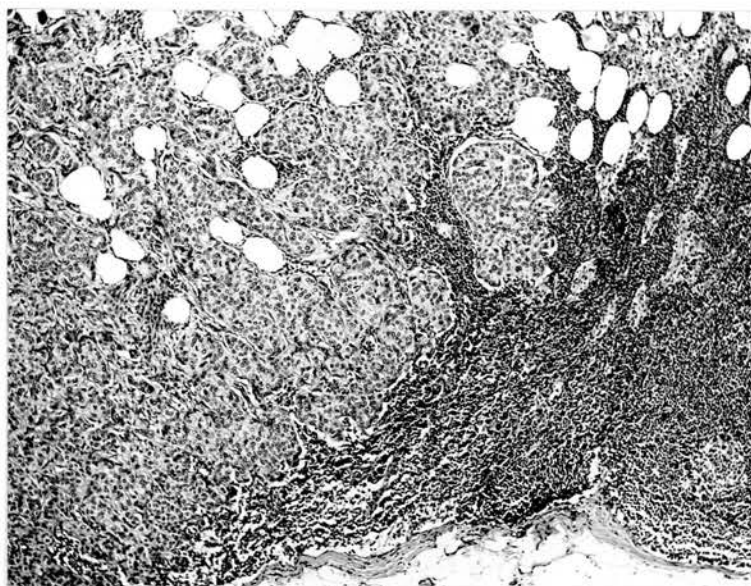


Fig. 290.

x 60.

Case 88.

1324.

History: The patient aged 69 noticed a painless lump in the breast only 3 weeks before examination.

Examination showed a circumscribed firm tumour 5 cm. in diameter (fig. 291) in the axillary tail. The preoperative diagnosis was carcinoma but there was some doubt about this at operation. The nipple was slightly retracted. Simple mastectomy was done as no palpable axillary nodes and no obvious abnormality were found elsewhere.

Histology: The tumour shows a defined spindle-celled fibrosarcoma (fig. 292), in general very cellular but without much pleomorphism though with considerable mitotic activity in many areas. There is no definite capsule. An unexpected finding was a small focus of carcinoma (fig. 293) so 9 further areas were taken for examination. The carcinomatous component shows considerable proliferative activity and infiltration (fig. 294). The peripheral sarcomatous tissue is invading the pectoral muscle (fig. 292) a segment of which was removed at operation. This is a recent case and the patient is alive and well exactly 1 year after operation. This "mixed tumour" is a carcinosarcoma possibly of collision type.

Case 88.



Fig. 291

x 1.

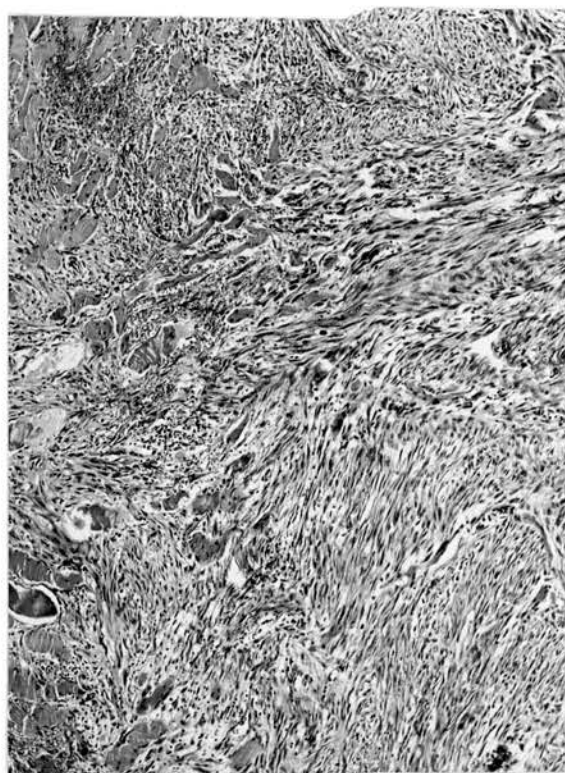


Fig. 292.

x 65.

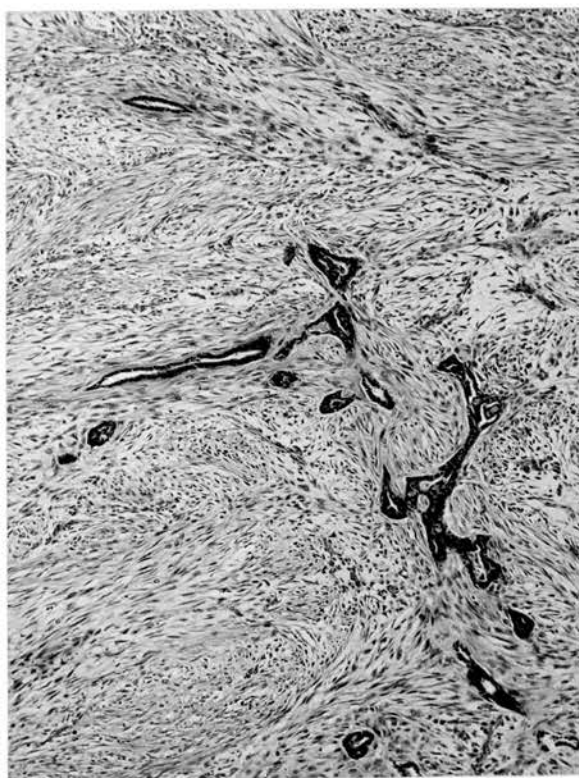


Fig. 293.

x 65.

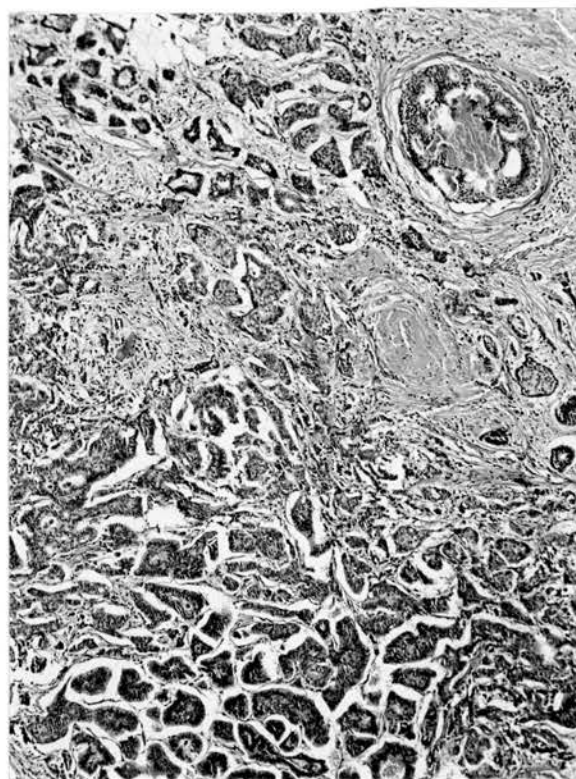


Fig. 294.

x 50.

Case 89.

S.151.

History: The patient aged 52 had noticed the tumour for 2 months.

Examination suggested a fibroadenoma and she was put on a waiting list.

Simple mastectomy was done followed by radical operation 14 days later when the report was received.

Histology: A carcinosarcoma with pleomorphic sarcoma and defined carcinomatous areas of squamous type (fig. 295).

The patient died 2 years 7 months after operation with metastasis in the brain.

Case 90.

1215.

History: The patient aged 37 found a painless swelling in the breast 1 month before admission to hospital. It had grown considerably since first noticed.

Examination showed a large oval swelling in the upper half of the breast, very hard with an almost smooth surface. It was not attached to skin or deep tissues and axillary nodes were not palpable. A radical mastectomy was done followed by irradiation. Two years later, there was marked oedema of the arm which improved after incisions. She was well, apart from some persisting oedema of the arm, exactly 5 years after operation.

Histology: This is a carcinosarcoma. The epithelium of partly squamoid type forms defined large and small masses in an active fibroblastic stroma (figs. 296 & 297). The lymph node is invaded by carcinoma only (fig. 298). There are many mitotic figures in both components but no appearances suggesting transition between them. No later notes are available.

Case 89.

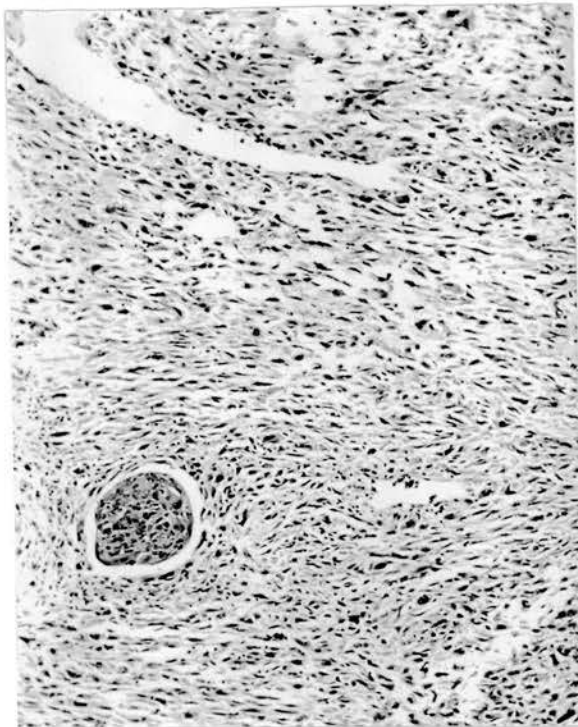


Fig. 295.

x 85.

Case 90.

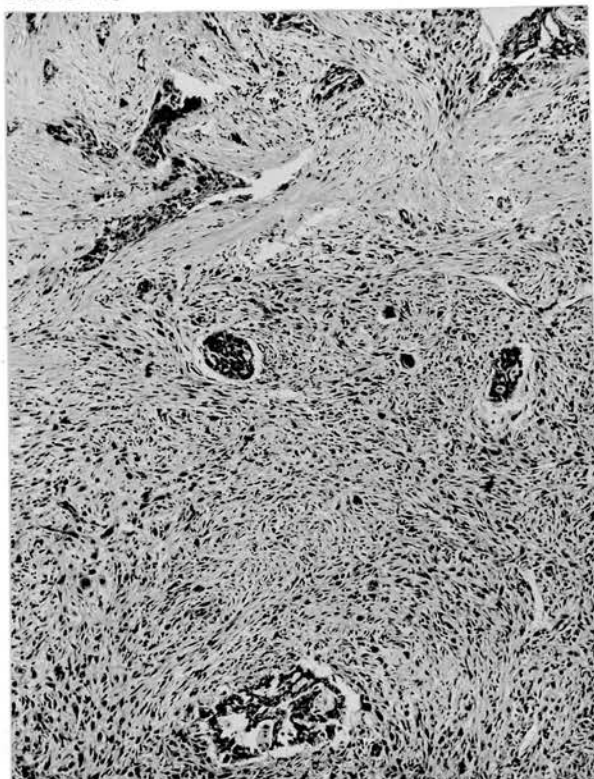


Fig. 296.

x 70.

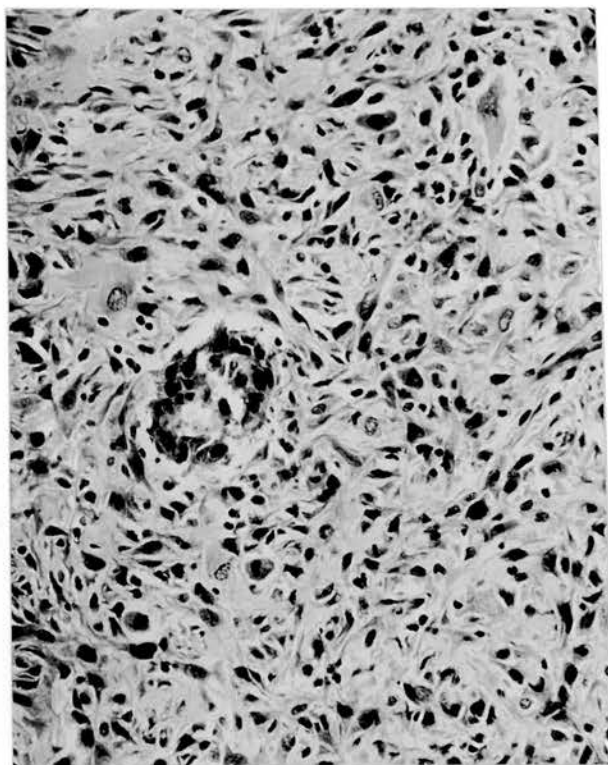


Fig. 297.

x 250.

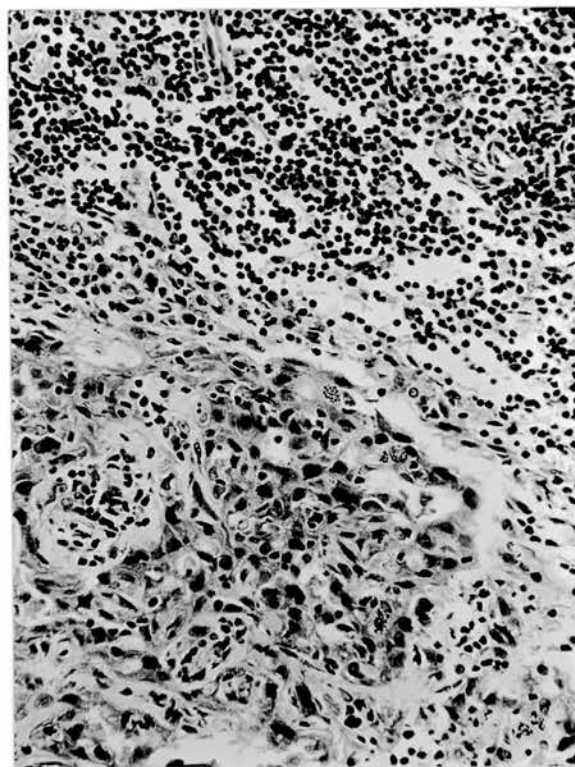


Fig. 298.

x 250.

Case 91.

S.144.

History: The patient aged 39 had a large tumour of unknown duration.

Examination: The tumour, size 7 x 6 cm. occupied most of the right breast. It was treated by irradiation but response was poor and a mass filled up the axilla. It responded well to stilboestrol but a residual nodule appeared in the scar and was later excised. She remains well 19 years after initial treatment, free from recurrence.

Histology: This is a carcinosarcoma of apparently "collison" type. The carcinoma is almost entirely intraductal, of small "comedo" duct structure (fig. 299). Solid strands of carcinoma are also embedded in the fibrosarcomatous stroma (fig.300) which is the predominant component and is active and mildly pleomorphic (figs. 301 & 303). An unexpected tumour structure is seen in (fig. 302), which resembles intra-epineural and extra-epineural proliferation of a neurosarcoma. But "even when a nerve is intimately associated with a malignant tumour, it does not necessarily follow that the growth arose within the nerve, since a fibrosarcoma or other mesenchymal sarcoma may engulf a peripheral nerve and infiltrate its epineurium" (Winston Evans). This circumscribed swelling, however, does suggest development within a nerve and therefore might be neural in origin, but no comparable formation was found elsewhere in the tumour, nor was there mention of stigmata of von Recklinghausen's neurofibromatosis.

Case 91.

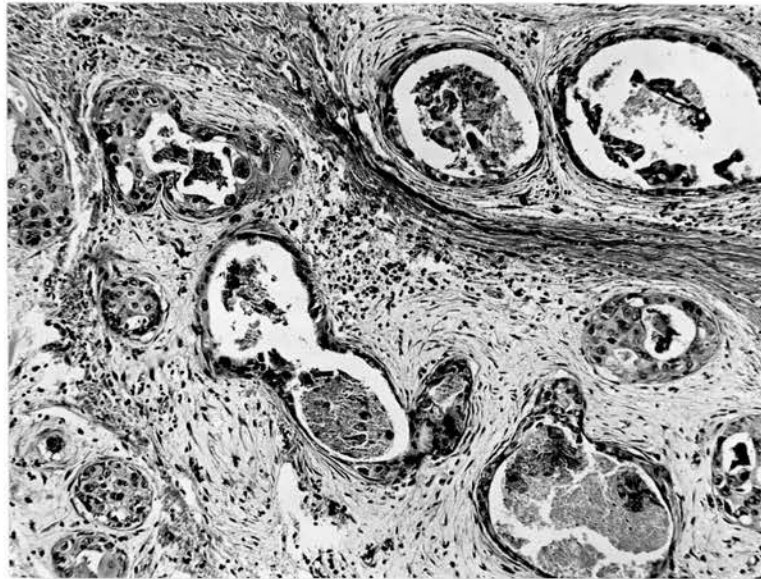


Fig. 299.

x 100.

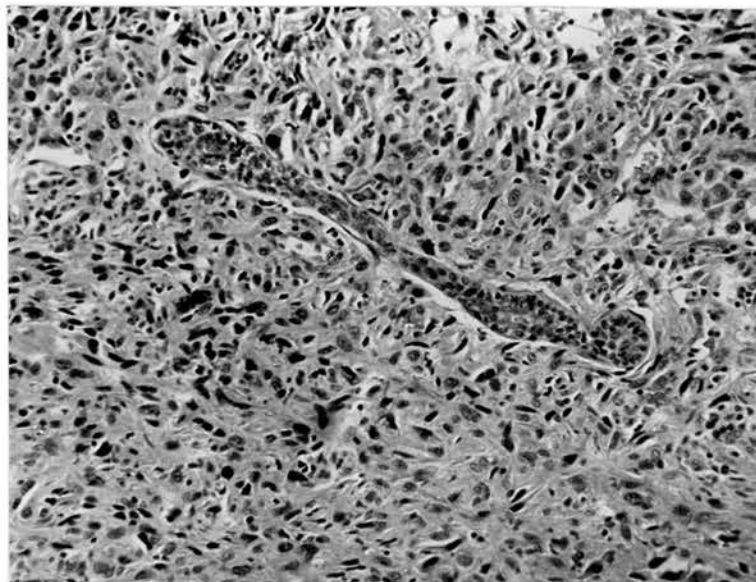


Fig. 300.

x 150.

Case 91.

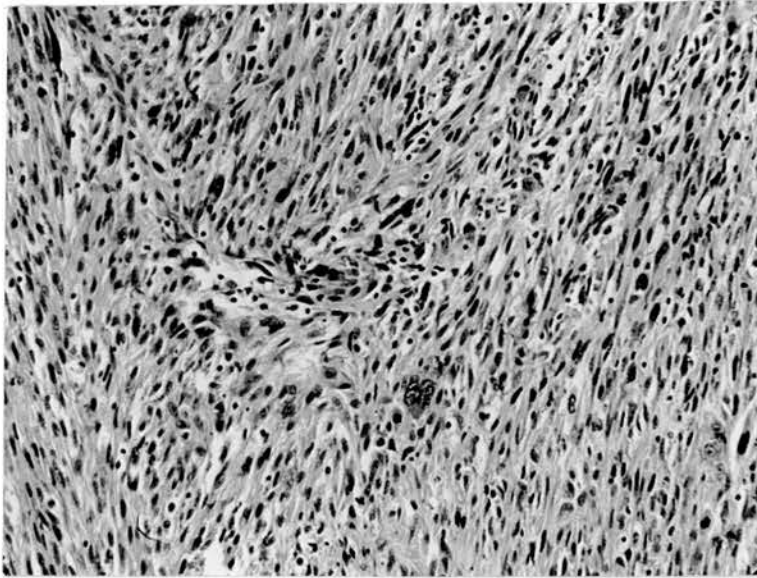


Fig. 301.

x 150.

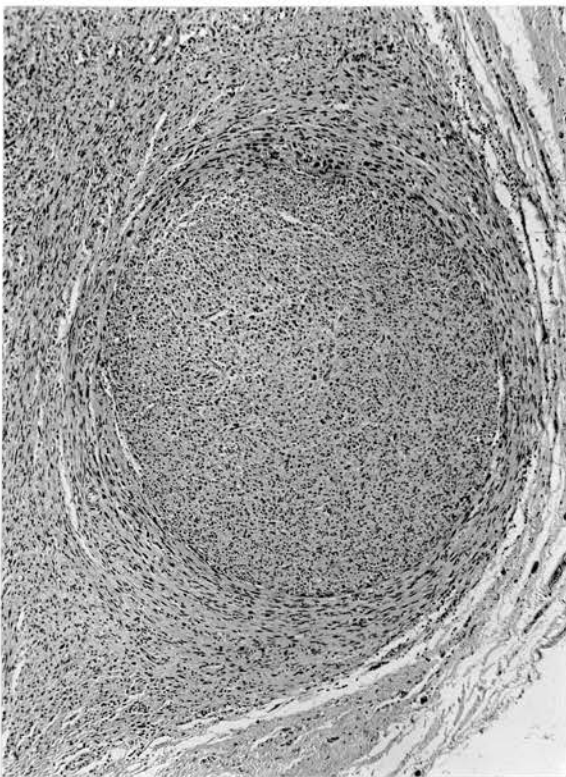


Fig. 302

x 50

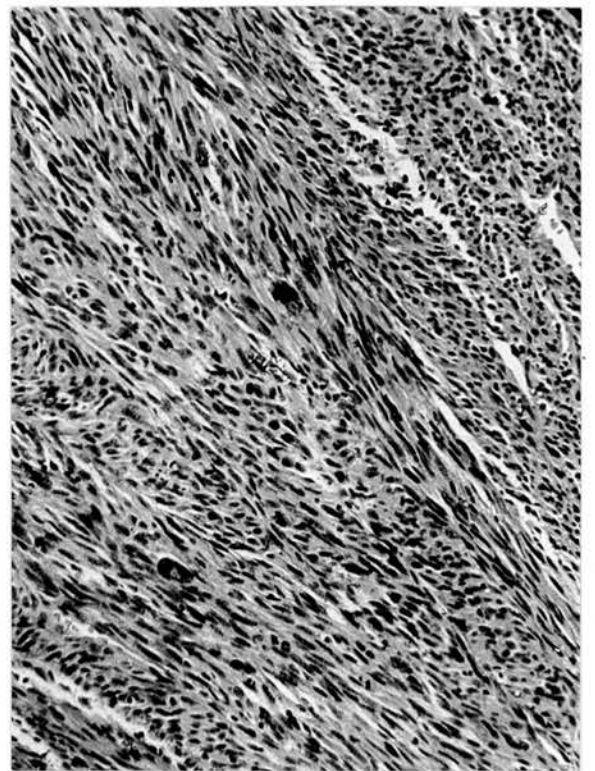


Fig. 303.

x 150.

For comparison with these mammary carcinosarcomas, a few similar tumours in other tissues are briefly described.

Carcinosarcoma of uterine cervical polyps.

Case 92.

694.

History: The patient aged 64, complained of uterine bleeding.

Examination: Uterine cervical polyps were found and a hysterectomy was done but the uterus and adnexae showed nothing abnormal for her age. A malignant polyp recurred in the groin 2 years 6 months later but the eventual outcome is not known.

Histology: A stained section of the polypoid tissue is shown in (fig. 304). It has a fibroadenomatous structure (fig. 305) with both components active and malignant. There are many mitotic figures in the covering epithelium (fig. 306) and many more in the fibroblastic stroma (13 in this high power field) fig. 307. This is a convincing carcinosarcoma derived from the fibroadenomatous growth.

Case 92.

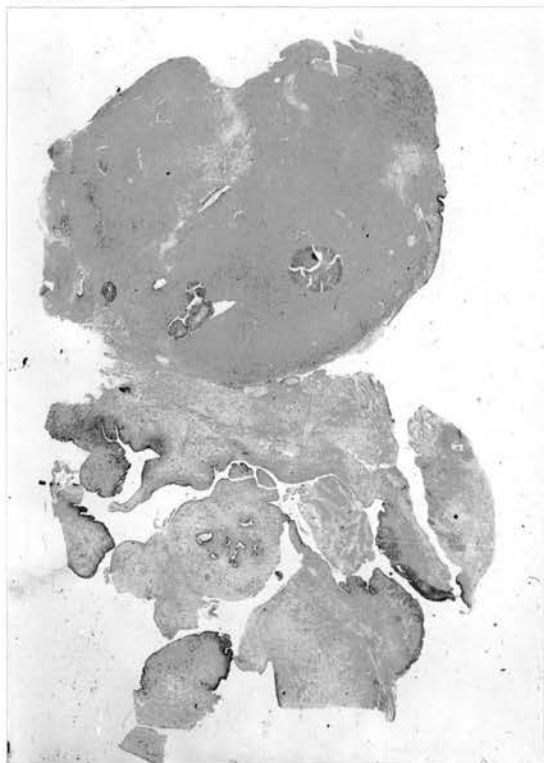


Fig. 304

x4.



Fig. 305

x50.

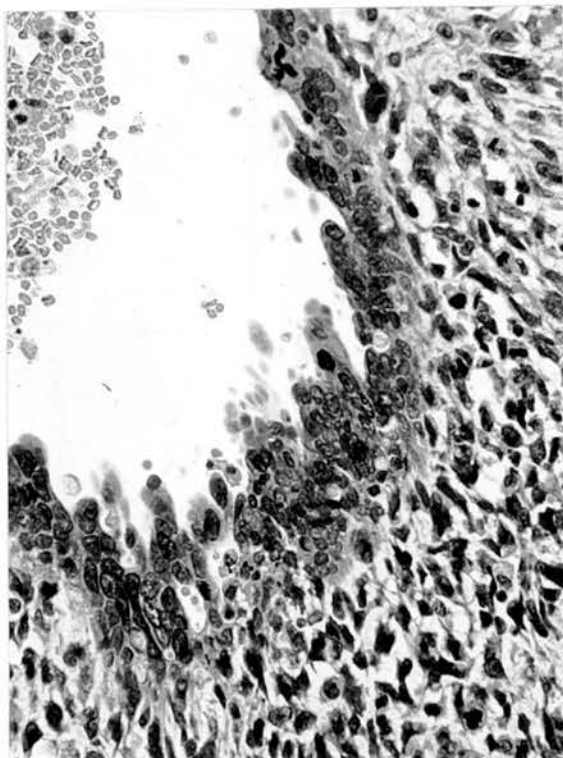


Fig. 306

x300.

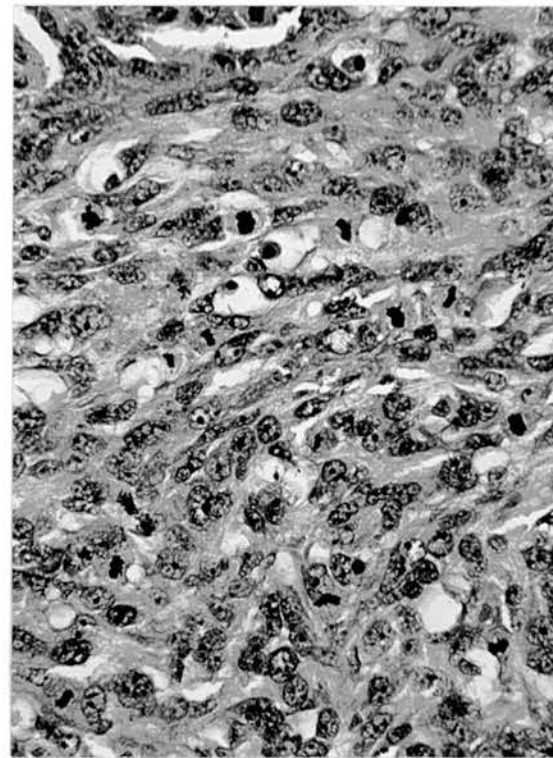


Fig. 307.

x300.

Carcinosarcoma of the kidney.

Case 93.

R.C.S. 219.

Carcinosarcoma of the kidney in a male patient of 75 years which had replaced most of the kidney substance. It recurred in the scar after nephrectomy with extensive abdominal metastases and was rapidly fatal.

Histology: The epithelial component was a squamous carcinoma derived from metaplasia of the lining cells of the kidney pelvis; the mesenchymal tissue was a fibrosarcoma producing numerous foci of malignant cartilage (fig. 308). At an earlier stage the combined tissues show areas of malignant fibroadenomatous structure (fig. 309).

Carcinosarcoma of the stomach.

Case 94.

R.C.S. 338.

Carcinosarcoma of the stomach forming a large polypoid tumour on the posterior wall in a male patient of 69 years. Small lymph nodes above the lesser curvature were invaded by both epithelial and mesenchymal components. The latter, as in the kidney described above, also showed malignant cartilaginous metaplasia. Fig. 310 shows a small reticulin-stained area of the gastric mucosa.

The kidney and the stomach are specimens in the Museum of the Royal College of Surgeons of Edinburgh.

Case 93.

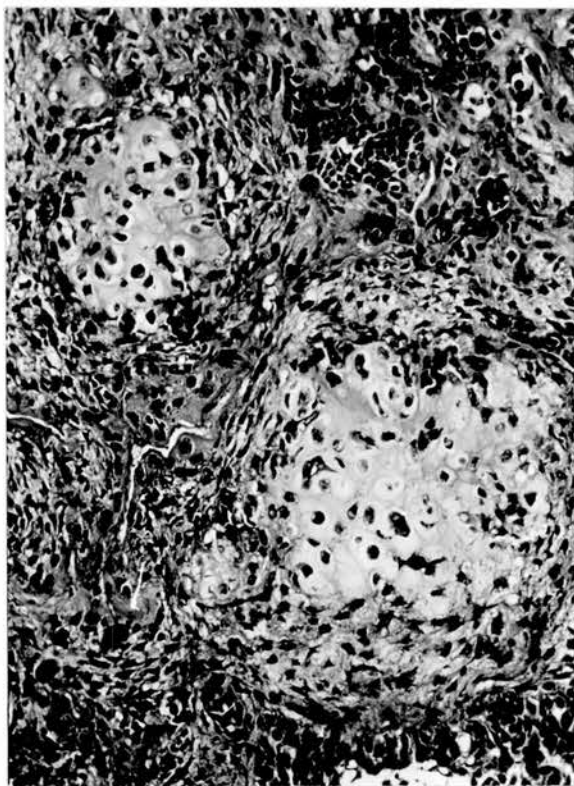


Fig. 308.

x 250.



Fig. 309.

x 100.

Case 94.



Fig. 310

x 140.

RARE AND DOUBTFUL

Cases 95 - 109. Figs. 311 - 353.

Other mesoblastic tumours

Other varieties of mesoblastic tumours occur in the breast with such exceptional rarity that it is unjustifiable to consider them as a series of groups. They are very occasional findings and are noted briefly in the subsequent paragraphs for record.

"Granular-cell myoblastoma"

Since Abrikossoff's original description of "Myoblastenmyome" (1926 and 1931), now generally described as granular-cell myoblastoma, the term has been enlarged to include a number of tumours which have no striped muscle derivation. The description granular-cell myoblastoma has thus acquired an uncertain and debatable significance. Reported cases include tumours of differing sites e.g. tongue, skin, bladder etc., and of varying type such as schwannomas, non-chromaffin paragangliomas (the so-called alveolar soft part sarcomas) and other tumours of organoid pattern. Willis (1967) would have the term "myoblastoma" discarded, as genuine malignant striped muscle tumours are rhabdomyosarcomas and the benign lesions (cf. Case 96) suggest muscle degeneration. But tumours of similar granular-cell structure in some sites have proved malignant and capable of metastasizing. Of the 13 cases of granular-cell myoblastoma tabulated by Mackenzie (1967) 10 of which developed metastases, 2 were in the breast and his own case had a mammary secondary deposit. Two other recent cases, both involving the oesophagus, a very rare site, have been reported by Wypkema et al. (1967).

Case 95.

1218.

History: The patient aged 42 years accidentally noticed a lump in the breast present for 7 weeks. It was tender on pressure but not painful; there was no discharge from the inverted nipple. No other relevant data were found.

Examination showed a very large breast with a small lump 2 x 1.75 x 1 cm. in the upper outer quadrant, like a thickening in the tissue. It was very firm, ill-defined, not fixed but not very mobile and not attached to muscle (fig. 311). No axillary nodes were felt; other breast was clinically normal. It suggested an early carcinoma and was locally excised but on transection appeared benign. It was reported as "unlike any

primary breast tumour and suggests a secondary deposit from a renal carcinoma." Pyelogram showed no filling defects though the kidney was ectopic, resting on the pelvic brim. She was alive and well 15 months later but untraced after that date.

Histology: This is a "granular cell myoblastoma" of characteristic structure, composed of sheets of large polyhedral cells with granular acidophil cytoplasm and a small hyperchromatic nucleus (figs. 312 & 313). The fibrous capsule shows a little early infiltration (fig. 314).

A similar but non-neoplastic lesion has also raised discussion and an example is briefly noted below.

Case 96.

320.

History: The patient aged 54 years had a mastectomy for a small lump 16 cm. lateral to the nipple, lying alongside pectoral muscle but suggesting a mammary tumour.

Serial sectioning of the breast tissue revealed no abnormality. A small portion of the pectoral muscle is incorporated within the periphery of the nodule which is firm and fibrous looking.

Histology: The cytology of the nodule is similar to the "granular cell myoblastoma" above, case 95, which was in the breast tissue, but in this case, transition between the granular cells and normal muscle is clearly demonstrated in figs. 315 & 316. This transition indicates an apparent degenerative lesion, not a neoplastic one.

The writer has observed similar histological appearances in pectoral muscle, with fibres partly or wholly granular, when compressed and disintegrating by invading mammary carcinoma.

Case 95.

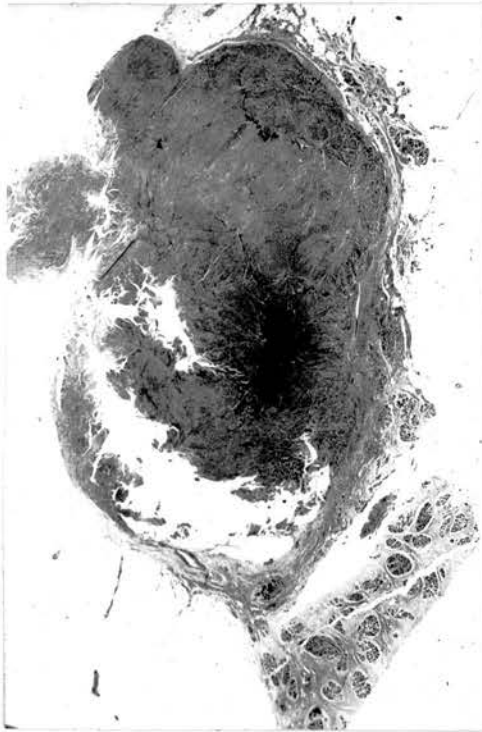


Fig. 311.

x6

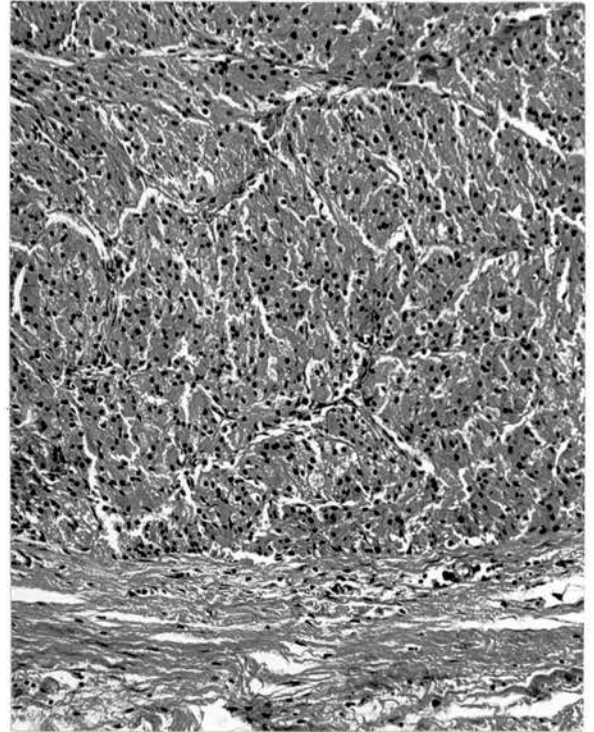


Fig. 312.

x100.

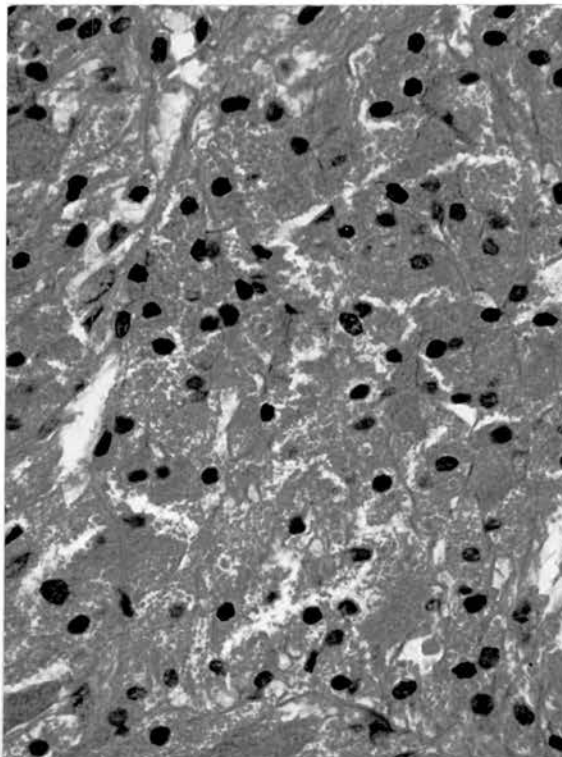


Fig. 313.

x475.

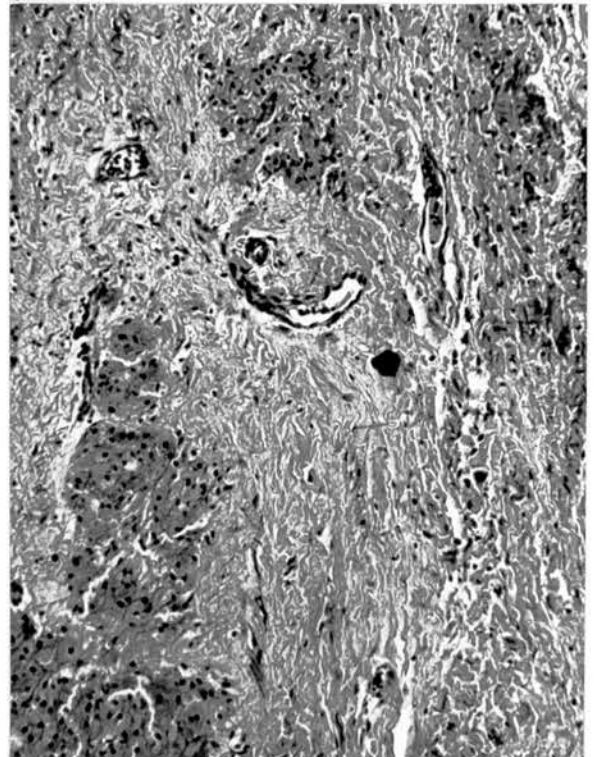


Fig. 314.

x140.

Case 96.

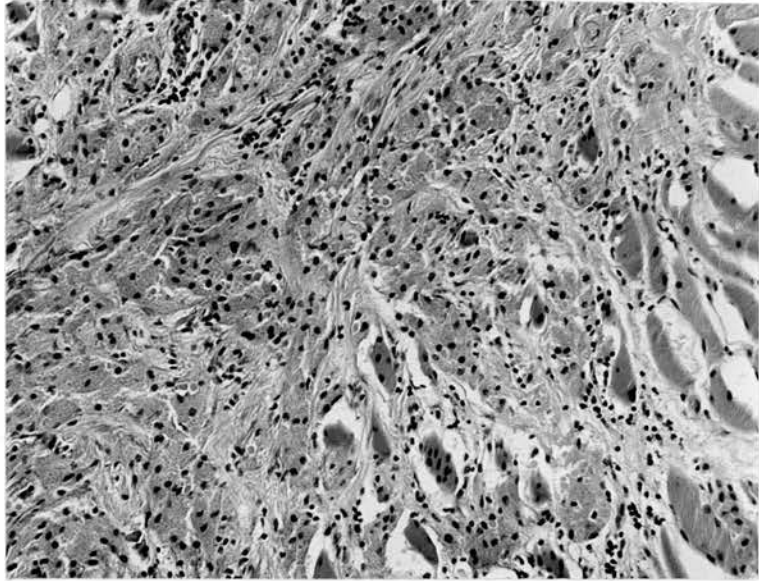


Fig. 315.

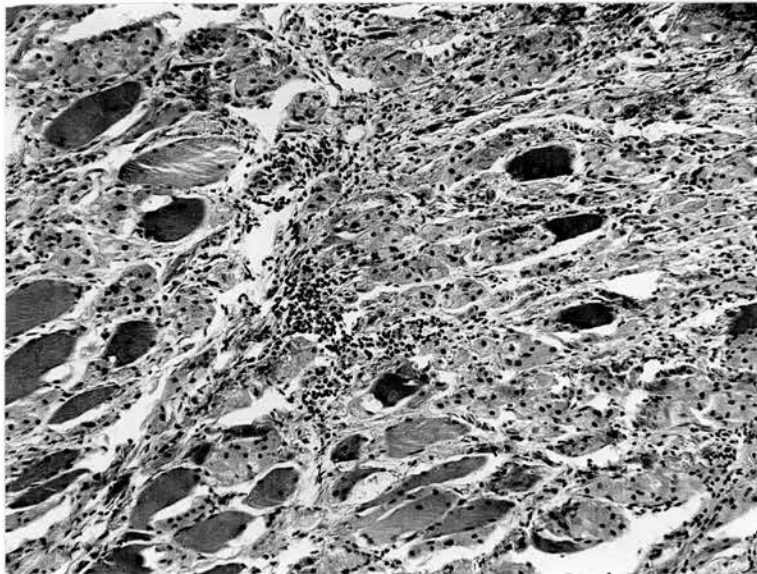


Fig. 316.

Neural Mammary Tumours

There are nerves of considerable size in mammary tissue but tumours arising from them are very rare.

Deaver & McFarland (1918) quote 2 cases described as neuromas in a French Medical Encyclopedia, 1870, but were doubtful of the diagnoses. They were unable to find mention of any other mammary neuroma in the literature. Lee (1927) reported a neurogenic sarcoma which recurred under the scar after 5 years, though he states that recurrence is found usually early after operation. Other neurogenic mammary tumours have been reported by Stewart and Copeland (1931), Fox (1934) and Sailer (1937). Cutler (1961) saw 2 cases, in children of 14 and 15 years, associated with von Recklinghausen's disease. The younger died after removal of the breast tumour with invasion of the lung. A traumatic ("stump") neuroma, developing after mastectomy, may be excised as a recurrent tumour. This is a very rare happening and only 2 examples have been personally examined.

Case 97.

S.100.

History: A patient aged 52. No other data available.

Examination showed an ovoid encapsulated tumour in the lower outer quadrant of the breast not attached to skin or muscle.

Histology: A benign neurofibroma, a rare tumour in the breast, showing the whorling of thin elongated cells; there were myxomatous areas elsewhere (figs. 317 & 318).

Case 97.

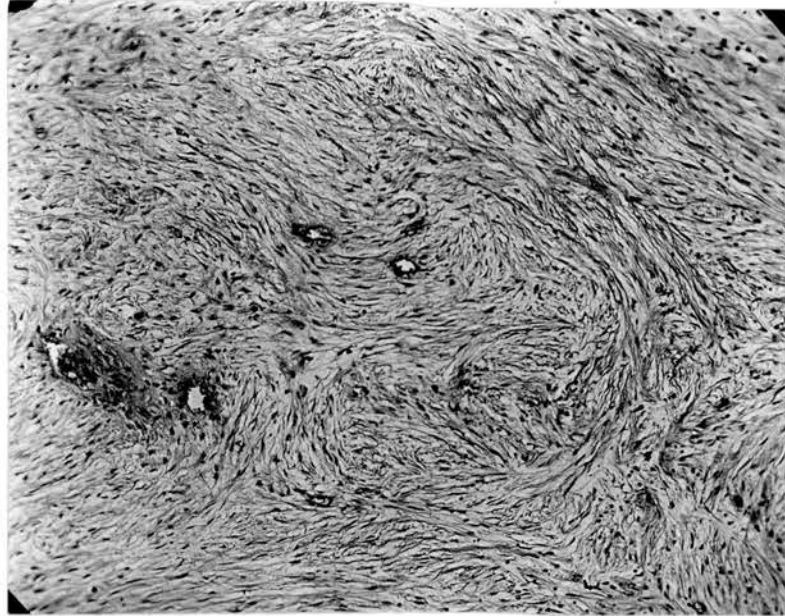


Fig. 317.

x 75.

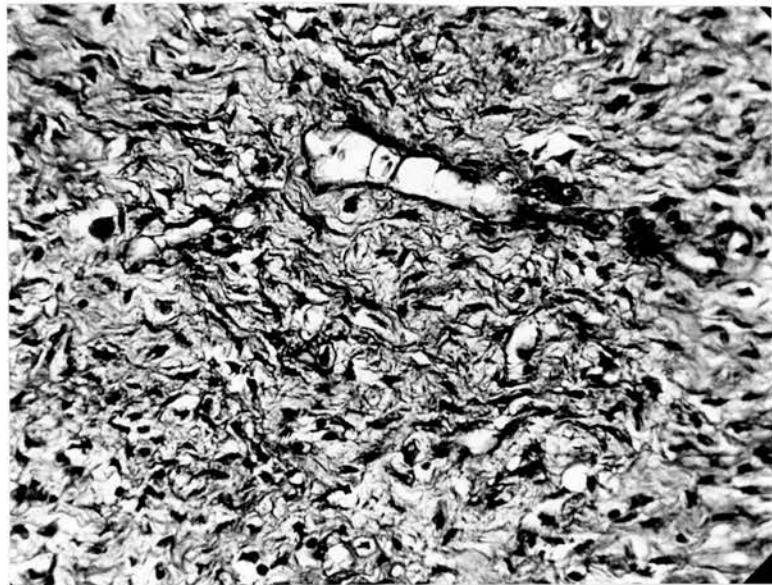


Fig. 318.

x 280.

Case 98.

S,72.

History: The patient aged 20 found a small tumour in the breast.

Examination: The clinical diagnosis was a benign tumour in the upper outer quadrant which on transection looked like a lobulated fibroadenoma with a myxoid stroma.

Histology: Many nerve twigs (fig. 319) and areas of cellular pleomorphic and hyperchromatic tissue (fig. 320), with some mucinoid areas. Characteristic fine parallel fibrillation tissue is seen at the periphery (fig. 321). This is considered a neurofibrosarcoma of low grade malignancy, likely to recur after the local excision but not to metastasize. No later note was available as she was in the Womens Auxilliary Services during the last war.

Case 98.

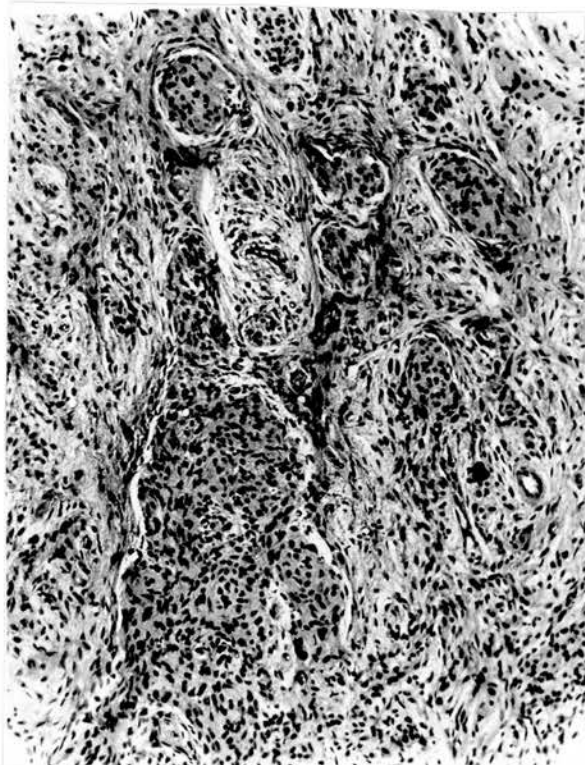


Fig. 319.

x100.

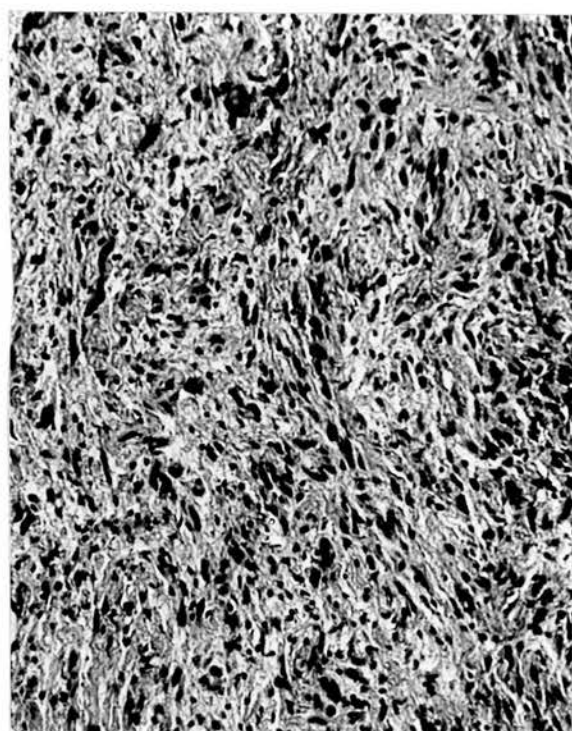


Fig. 320.

x160.

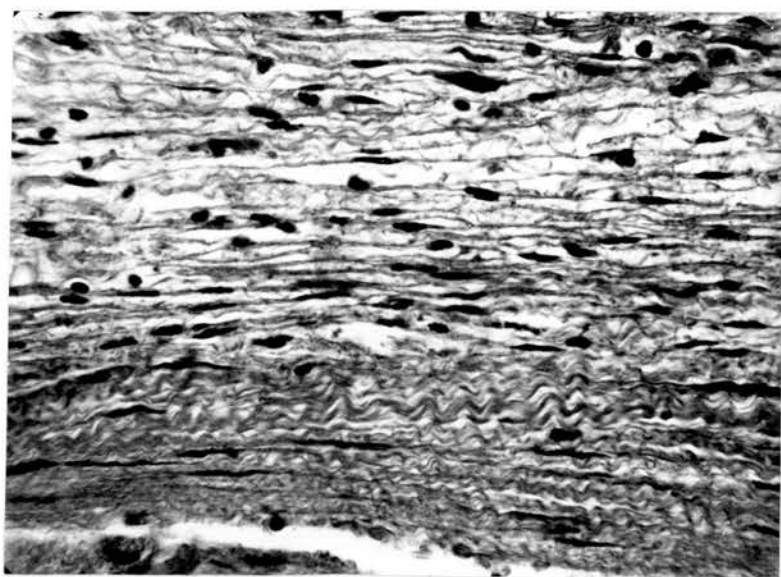


Fig. 321

x400.

Metastatic Tumours.

Metastatic sarcoma of the breast is rare apart from the lymphomas and leukaemic deposits. Sandison (1957) reviewed a personal series of 357 autopsies on patients with sarcoma; 20 demonstrated breast metastases. In a later paper (1959) he reported nine surgical cases of leiomyosarcomas of which in one instance there were mammary metastatic deposits. His experience suggests that "the routine examination of the breasts at tumour autopsies would greatly increase the known incidence of metastatic tumour in the breast".

My personal experience is limited to 2 cases.

Case 99

1138.

History: The patient, a woman of 62 years, noticed a painless lump in the breast for 3 weeks.

Examination: Clinically, it suggested cystic hyperplasia ("chronic mastitis") and was locally excised. It recurred 10 months later and was again excised. At the second recurrence, 1 year and 3 months after the first excision, a mastectomy was done and X-rays revealed a bone tumour.

Histology: This is a myeloma of plasma cell type. The first operation tissue (fig. 322) shows a closely cellular myeloma, in which are embedded small mammary ducts and large fat cells. The second operation tissue (fig. 323) shows a similar myeloma deposit with foreign body giant cells associated with irregular amyloid areas recognised by methyl violet staining. The characteristic myeloma cell is seen in the third operation tissue (fig. 324) with closely packed plasma cells with some variation in size and considerable mitotic activity.

This metastatic involvement of mammary tissue implies dissemination of a primary bone myeloma and a fatal outcome, the date of which was not given.

The second example of metastatic mammary tumour was from a leiomyosarcoma of the uterus. The clinical data are not available.

Case 99.

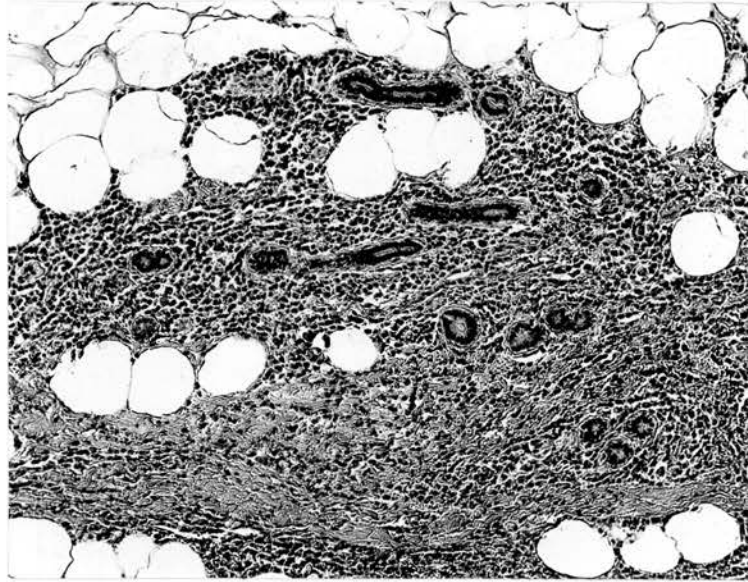


Fig 322.

x 100.

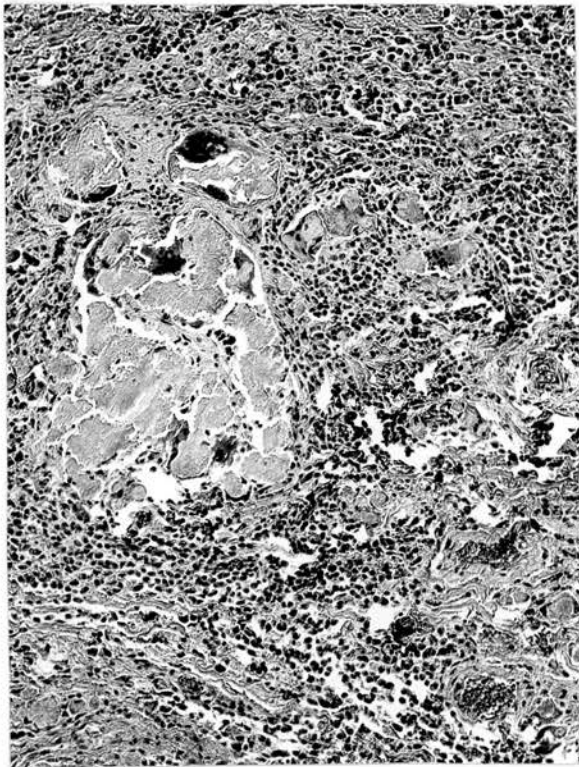


Fig 323.

x 100.

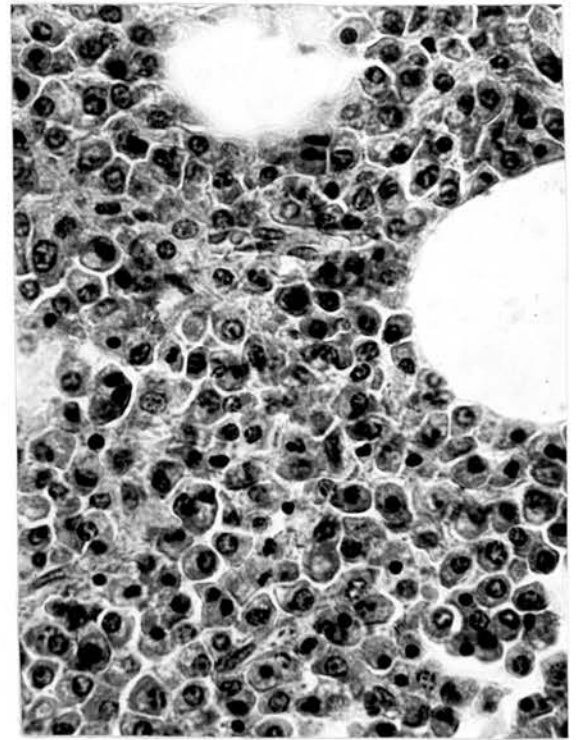


Fig 324.

x 475.

Case 100.

S.11.

History: The patient aged 64 had noticed the tumour for 3 months. A radical mastectomy was done.

Examination: The breast was largely fat with a small hard tumour which on transection suggested a scirrhus carcinoma (fig. 325). No nodes were found in the axillary tissue.

Histology: Much of the tumour is fibroblastic with fasciculated spindle-cells especially where it is invading the mammary fat (fig. 326). A few ducts remain (fig. 327) but some areas have a curious fenestrated structure shown at different magnifications in figs. 327, 328 and 329. These "spaces", less prominent in the cellular areas (fig. 330) are difficult to interpret. The detached cells of varied type in and lining the spaces might be blood cells? No later history available.

Case 100.

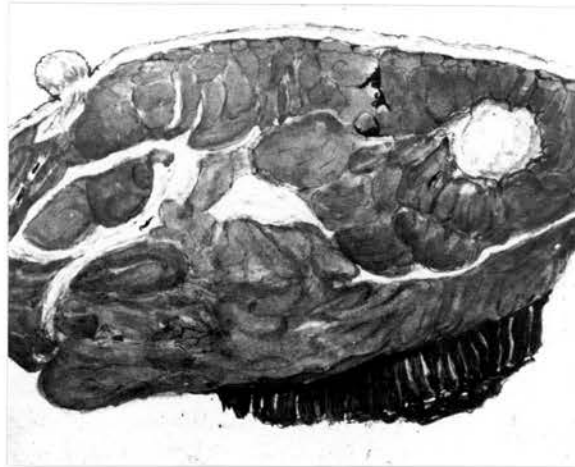


Fig. 325.

x 2/3.

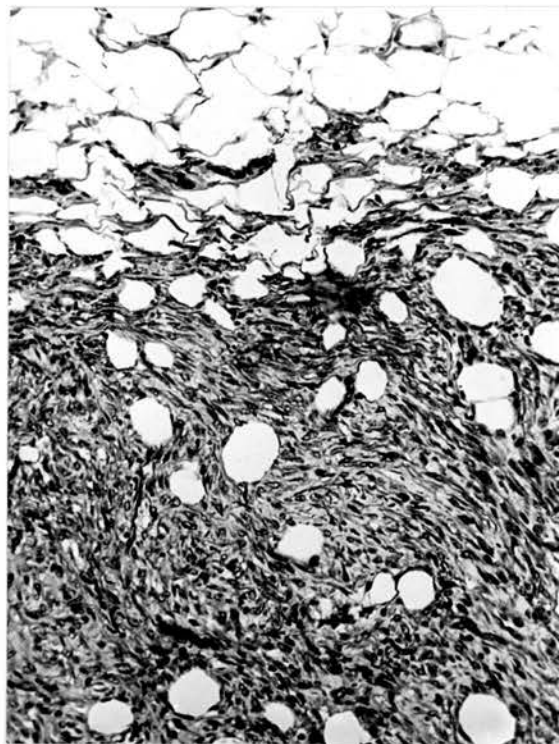


Fig. 326.

x 120.

Case 100.

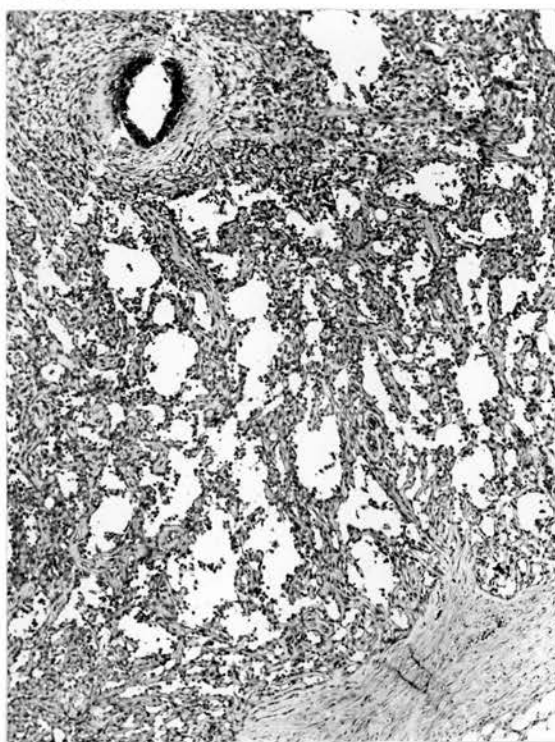


Fig. 327.

x55.

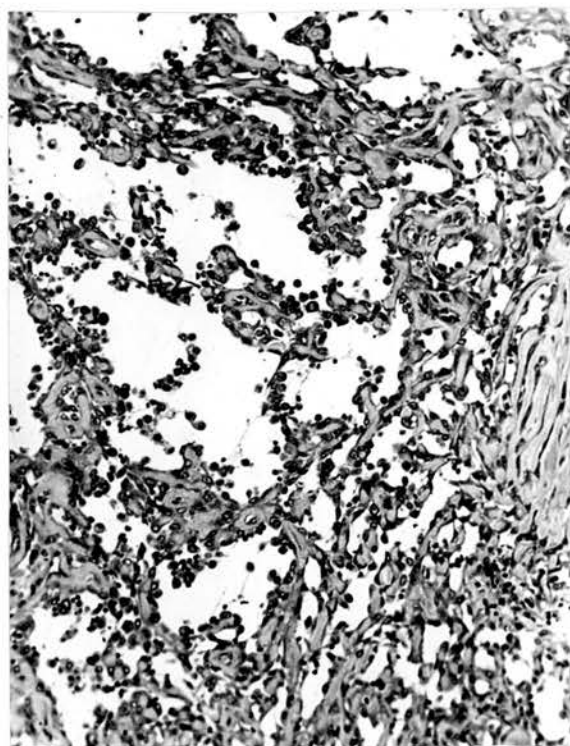


Fig. 328.

x130.

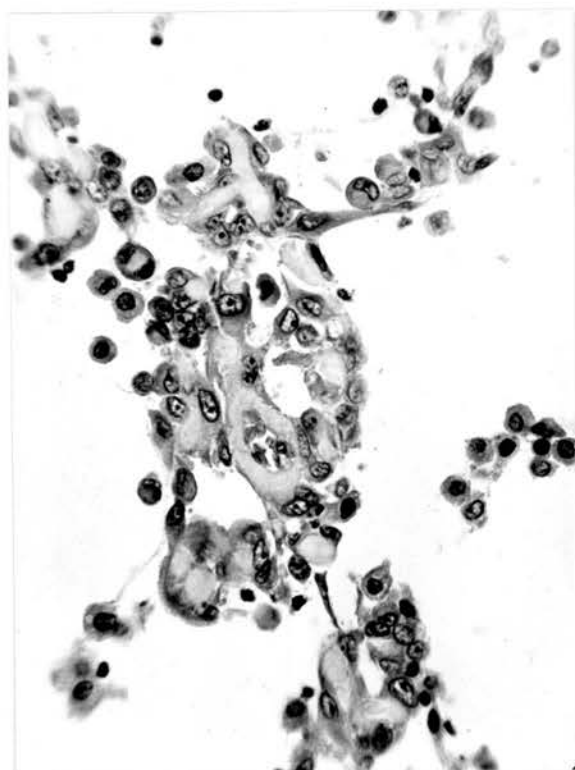


Fig. 329.

x400.

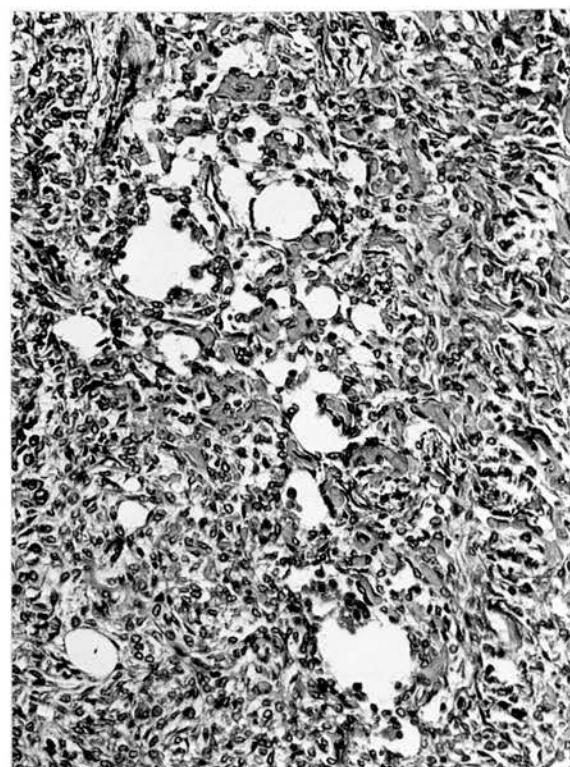


Fig. 330.

x150.

Case 101.

S.113.

History: The patient aged 64 had noticed a lump in the breast for 3 weeks. She had had a blood-stained nipple discharge 20 years previously.

Examination showed a large mass protruding in the upper outer quadrant and attached to nipple and to skin in places. No lymph nodes were palpable. It was sent with a diagnosis of "probably sarcoma in a fibroadenoma" and radical mastectomy was done. Other pathologists thought it was an unusual form of carcinoma.

Histology: On transection a circumscribed almost encapsulated tumour 4.5 cm. in diameter with early small "cyst" formation was seen. Much of the tumour shows small elongated cavities suggestive of vascular spaces lined by flattened or protruding cells, with a few loose cell contents (figs. 331, 332). These lining cells appear to be continuous with a meshwork of similar cells outside the spaces which infiltrate a poorly cellular stroma and look epithelial (figs. 333 & 334). There is a definite capsule (fig. 333).

Eight months after mastectomy the patient had a haemoptysis and later, shadows were found in the lung. She died in the 2nd year after operation with pulmonary metastasis.

This may be an unusual type of carcinoma suggested by the infiltrative growth in (figs. 333 & 334) but the absence of axillary invasion and the structure in figs. 331 & 332 admit other possibilities.

Case 101.

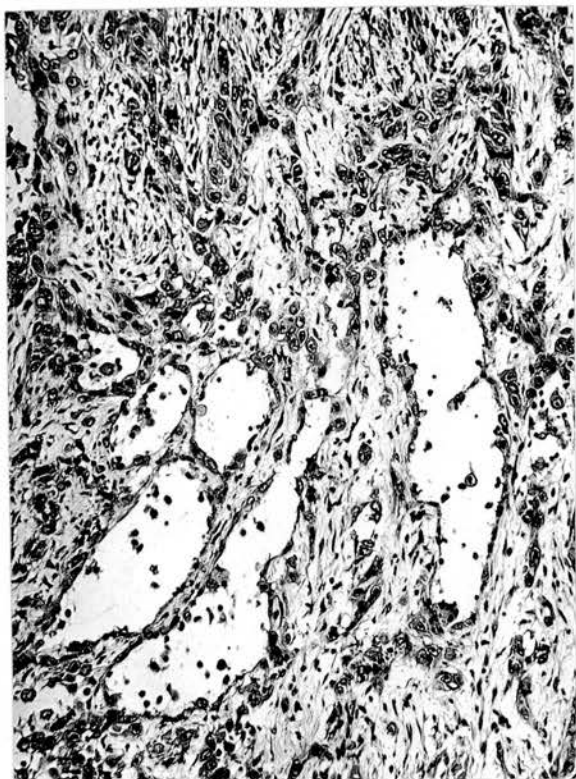


Fig. 331.

x 100.

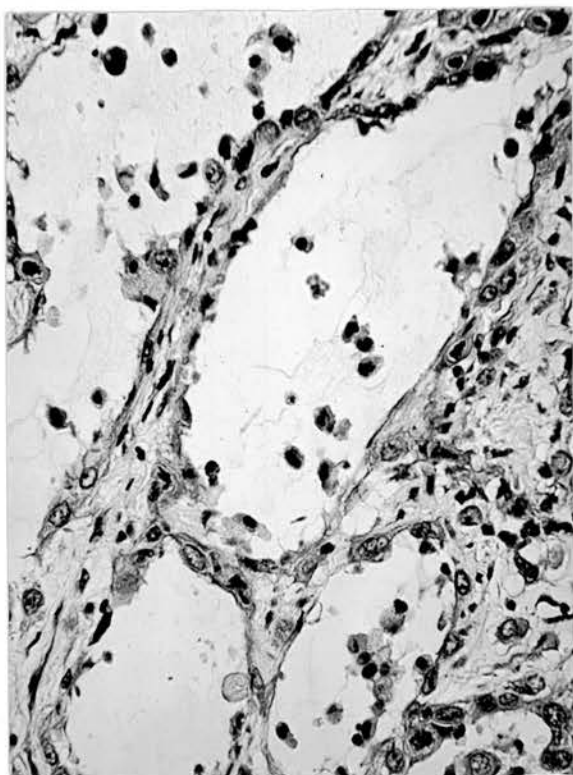


Fig. 332.

x 275.

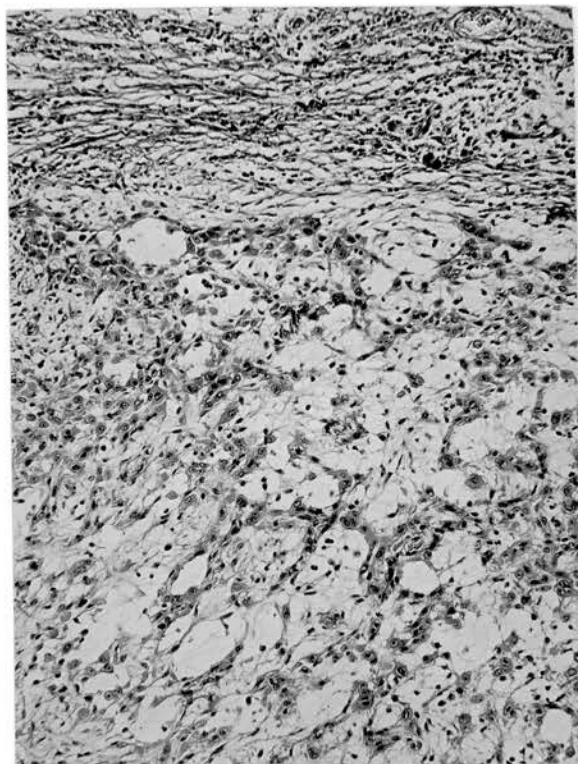


Fig. 333.

x 100.

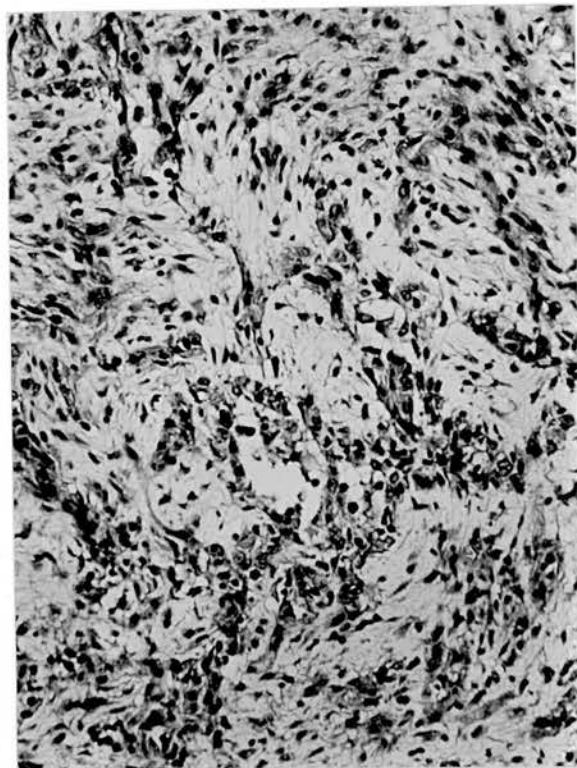


Fig. 334.

x 160.

Case 102.

- Fig. 335. Biopsy tissue from a mammary tumour suggestive histologically of sarcoma.
- Fig. 336. Same, more tissue examined, definite squamous cell carcinoma, a rare mammary tumour.
- Fig. 337. Axillary lymph node, with mainly carcinomatous structure, with some spindle cells.

Case 103.

Cyst of breast - woman aged 59.

- Fig. 338. Cyst wall (left) of squamous carcinoma with some infiltration below.
- Fig. 339. Same, deep to wall, spindle-cell area of infiltration.
- Fig. 340. Same, with scattered large cells.

Case 104.

Cystic fibroadenoma, woman aged 21.

- Fig. 341. Benign cystic fibroadenoma, with small keratinized downgrowth cyst.

Case 105.

- Fig. 342. Carcinomatous fibroadenoma, woman aged 57, showing complete separation of epithelial and mesoblastic components.

Compare series of these tumours, cases 78 to 86, figs. 263 - 285.

Case 102.

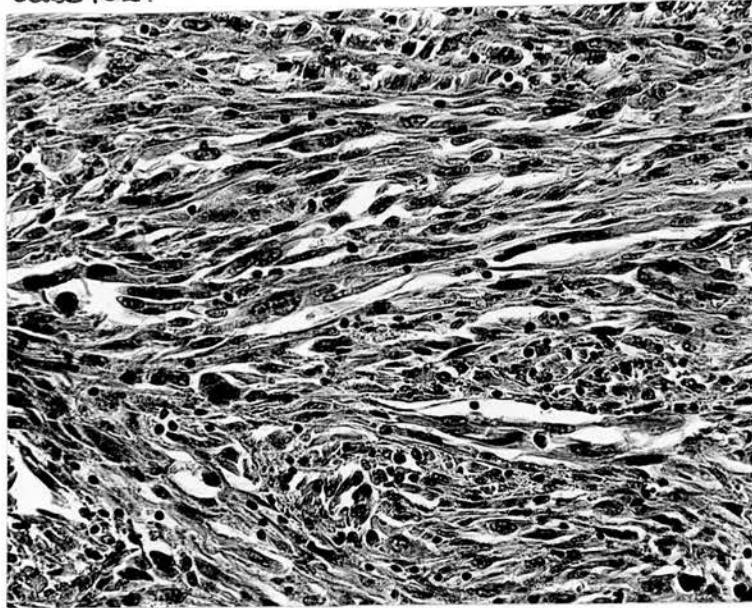


Fig. 335.

x 250.

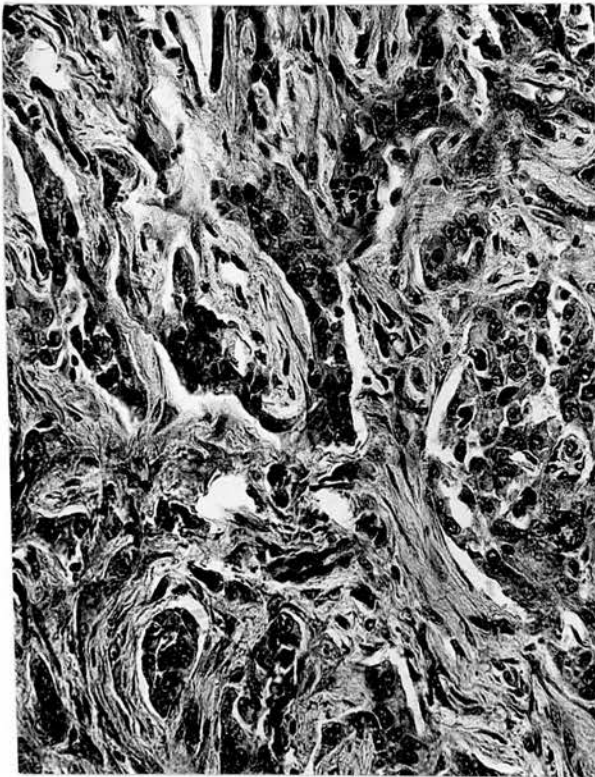


Fig. 336

x 250.

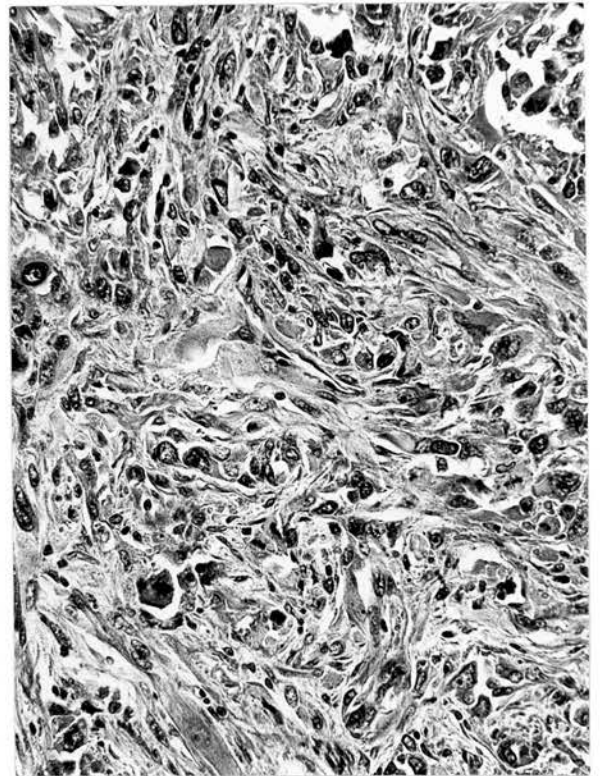


Fig. 337.

x 250.

Case 103.

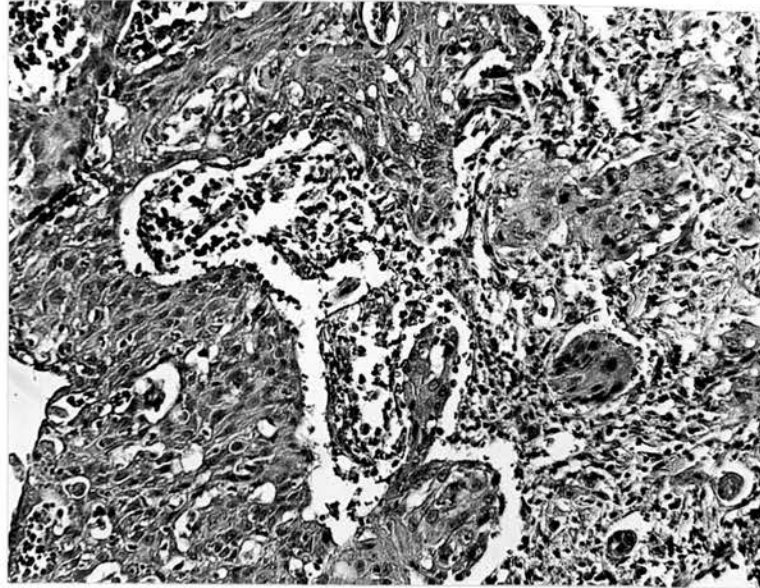


Fig. 338

x 150

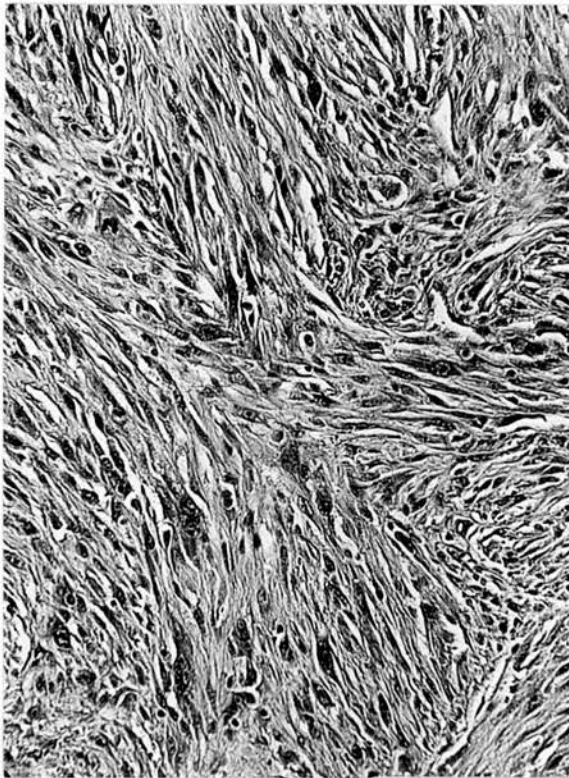


Fig. 339.

x 150.

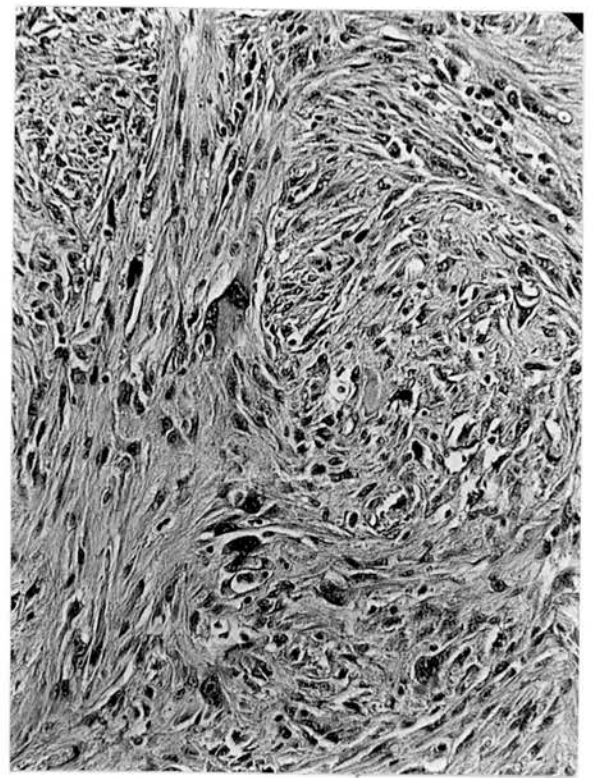


Fig. 340.

x150

Case 104.

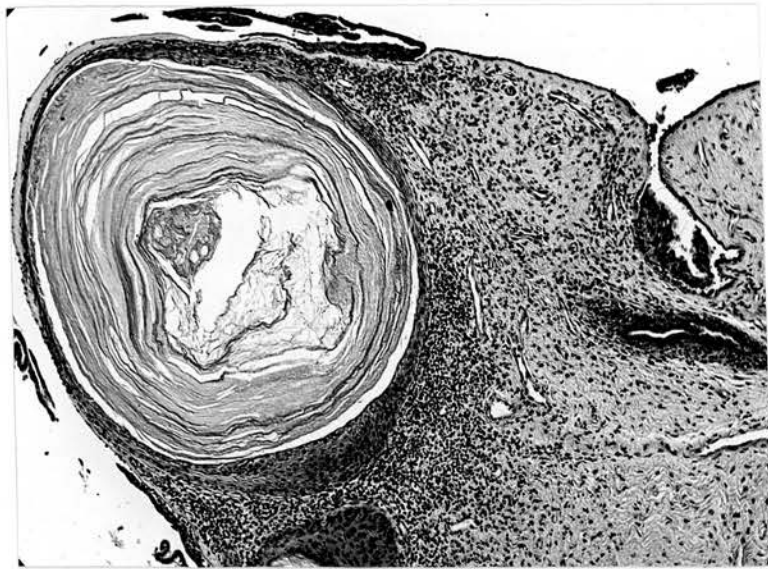


Fig. 341.

x75.

Case 105.

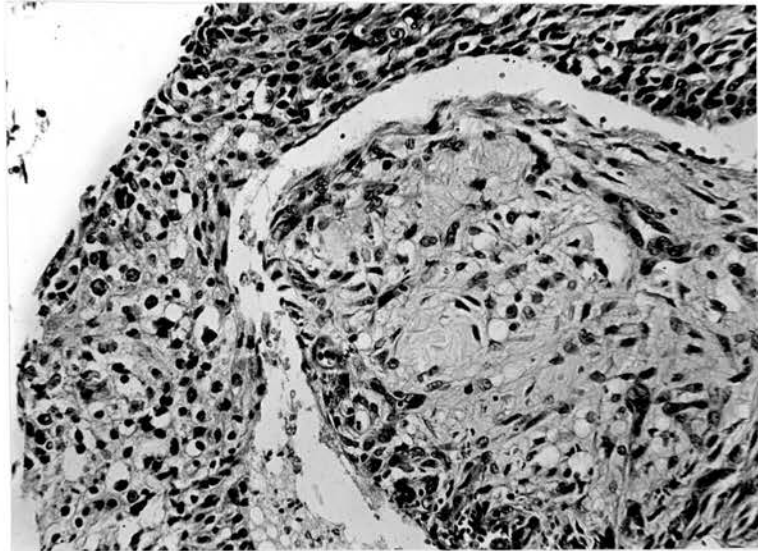


Fig. 342.

x225.

3 cases showing necessity of adequate tissue examination.

Case 106.

Woman aged 51. Died 18 months post-operation, with mediastinal metastasis.

Fig. 343 Large area of breast to show varied histology.

Fig. 344 Diagnosed as sarcoma, on ^{upper} lower area.

Fig. 345 Same, rather indefinite diagnosis.

Fig. 346 Same, with intracystic malignant papilloma, left hand area as in Fig. 343.

Fig. 347 Same, an unexpected picture, in upper tumour area, highly pleomorphic.

Case 107.

Woman aged 62, whole breast section.

Fig. 348 Not a diagnostic structure per se.

Fig. 349 Same, to show histogenesis and spread of carcinoma.

Case 108.

Woman aged 42.

Fig. 350 Not a diagnostic structure, per se.

Fig. 351 Same, an obvious cellular carcinoma.

Case 106

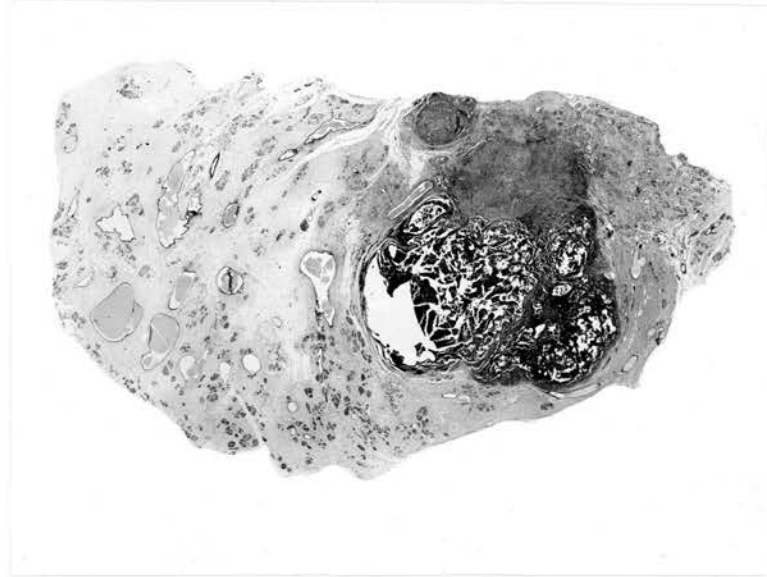


Fig. 343.

$\times 2/3$.

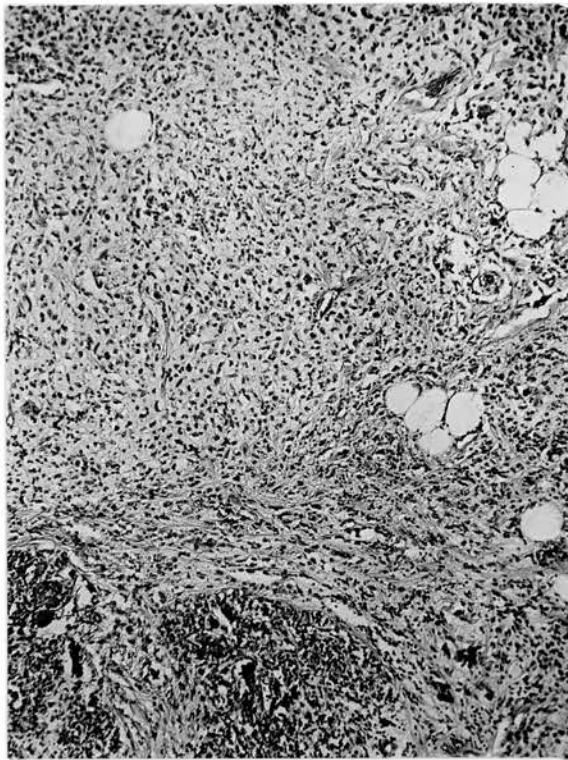


Fig. 344.

$\times 70$.

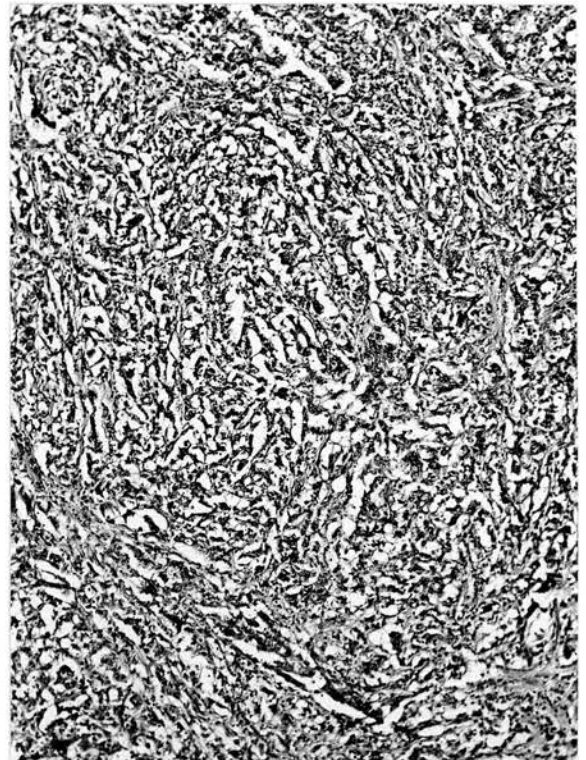


Fig. 345.

$\times 70$.

Case 106.

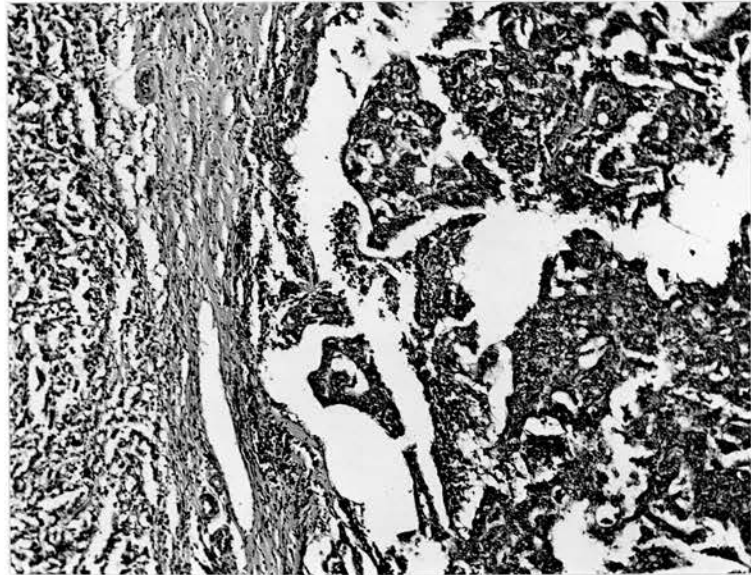


Fig. 346.

x70.

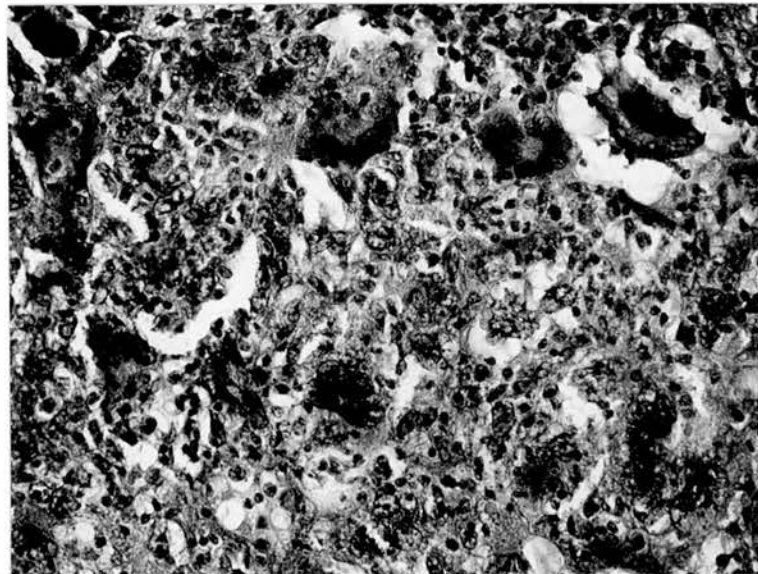


Fig. 347.

x250.

Case 107.

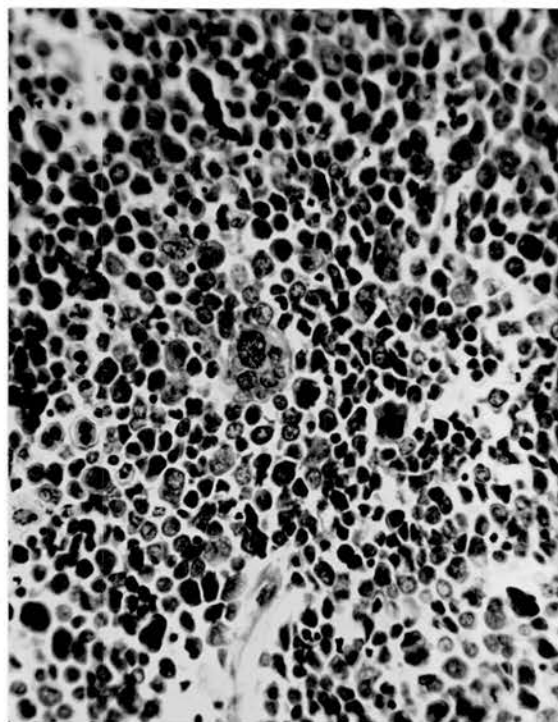


Fig. 348.

x250.

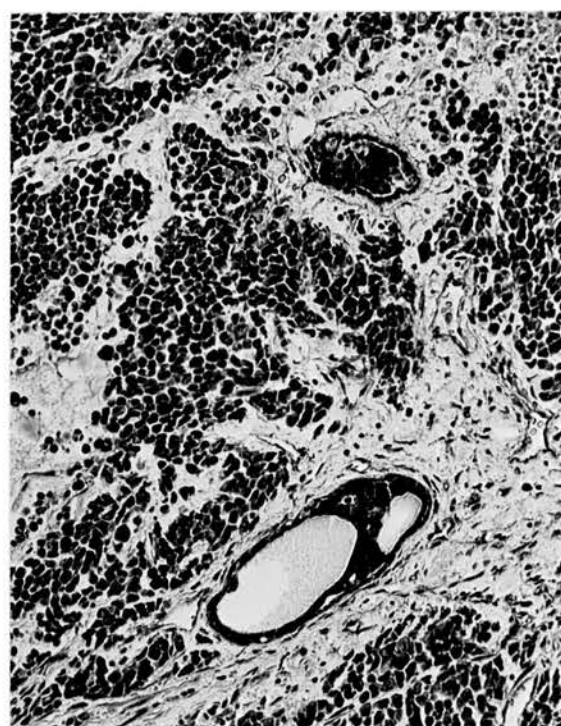


Fig. 349.

x150.

Case 108.

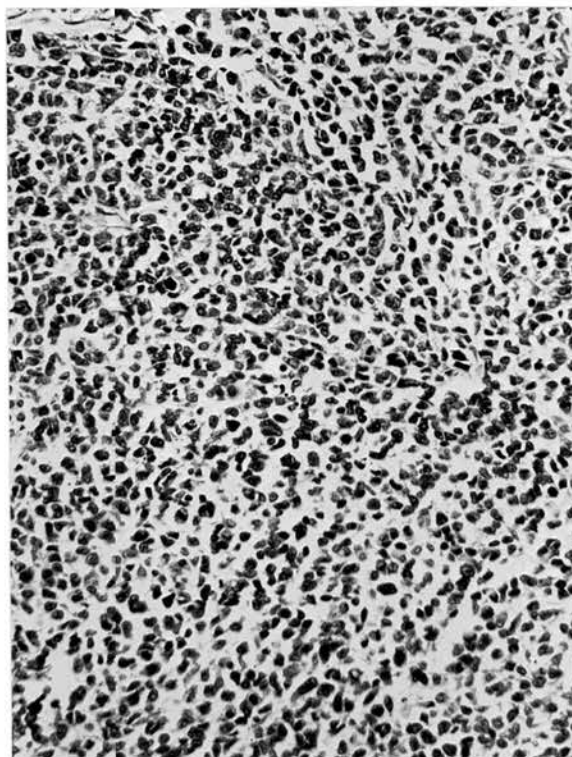


Fig. 350.

x150.

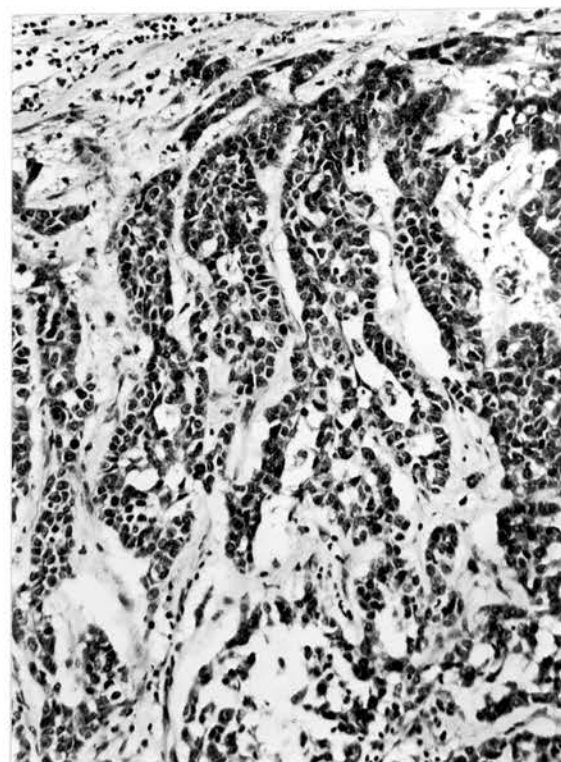


Fig. 351.

x150.

One needs to be reminded occasionally that a primary tumour may be followed by a neoplasm of quite different histogenesis and workers at irradiation centres, where patients are particularly carefully followed, tell me this sequence is not a rare event. Lawrence (1955) reported a bilateral mammary malignancy, carcinoma and sarcoma, followed later by an ovarian carcinoma which proved fatal. Other cases are in the literature.

The following case is also instructive.

Case 109.

787.

History: A patient aged 80 complained of a lump in the left breast noticed for 2 - 3 months and painless.

Examination: The tumour was fixed to the skin but not to deeper structures. No palpable lymph nodes present. Simple mastectomy was followed by radiotherapy.

Histology: A scirrhous carcinoma of glanduliform type (fig. 352). No metastases found on radiography.

Nine months later a nodule was observed in the subcutaneous tissue of the left iliac fossa; the skin was fixed and reddened over it. Examination of the excised tissue showed a highly vascular nodule consisting almost entirely of soft creamy tissue.

Histology showed a cellular pleomorphic malignant growth with many bizarre multinucleated giant cells. No further treatment given.

Two years 10 months later, a swelling was noted beneath the scar of the second operation and a lump was excised. The surgeon thought it was completely removed and might be a lipoma. It showed the same structure as the previous nodule (fig. 353). Both are liposarcomas and fat-staining is strongly positive with Sudan III in the large anaplastic cells. No later outcome available but no evidence of recurrence of the mammary carcinoma 3 years 7 months after its removal.

Case 109.

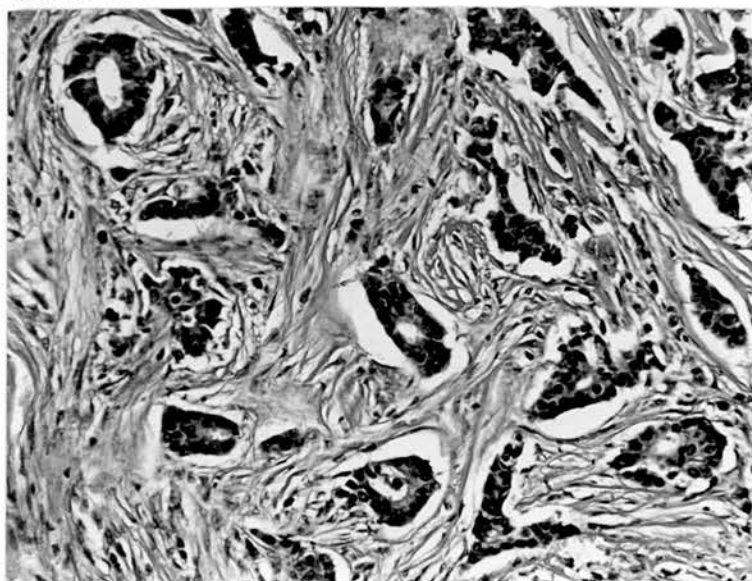


Fig. 352.

x150



Fig. 353.

x150

Lymphomatous tumours of the breast.

In the series of mammary sarcomas I have studied, a number of cases occur in which the malignant cell type clearly indicates an origin from lymphoid tissue. The difficulty in these cases is to differentiate those which arise primarily in the breast and those which are secondary deposits from a lymphoid tumour elsewhere or evidence of a leukaemic condition of the blood. The data at my disposal for the exclusion of lesions in other tissues is inadequate and I have therefore excluded these from this review.

The normal lymph node shown in fig. 354 was excised with an area of cystic hyperplasia of the breast, evidence that malignant lymphoid tumours of various types may occur as a primary tumour in the breast. Stiles found that axillary lymph nodes increase in number during pregnancy, a finding which indicates that new nodes may be formed in adult life. This suggests that they may occasionally develop de novo in other than the usual sites. In mammary lesions in which deposits of normal lymphocytes accumulate, active lymphoblastic activity may develop and eventually form small lymph nodes in the breast.

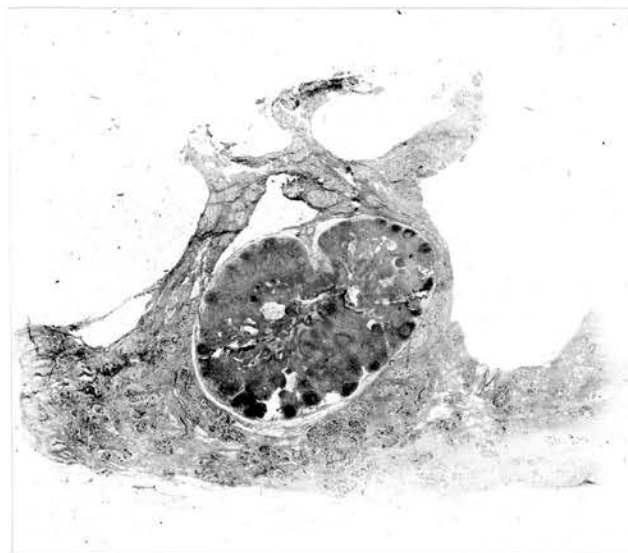


Fig. 354.

MYOTHELIUM

HUMAN - Figs. 355 - 375.

CANINE - Figs. 376 - 388.

"Myoethelium" ("Myoepithelium") in Human & Canine Tumours.

The term used in human pathology is "myoepithelium" (Biggs. 1947) or "myoepithelial complex" (Bonser et al. 1961). I have used "myoethelium", as is more usual in veterinary pathology, a term which does not initially prejudge its nature and function. The problem of myoethelium arises from its position in the glandular structures below the epithelial lining layer but inside the basement membrane, hence its description as myoepithelium. It is also called the "interposed cell", a term which again leaves its nature undecided, while defining its normal position.

Several questions need brief consideration in regard to myoethelium in human and canine mammary tissue, though it is found also in salivary gland tumours (cf. fig. 370) and in sweat gland tumours ("apocrine myoepithelioma") where it may be irregularly elongated and proliferate in sheets (Winston Evans 1967) cf. fig. 377. Allen (1940) noted a striking difference in comparative pathology, recognised but unexplained, in the remarkably high incidence of cartilage and bone in canine mammary tumours as contrasted with human tumours. I have found no definite figures of this high incidence in bitch tumours, but bone and cartilage may be more frequent in human fibroepithelial growths than is usually recognised. This problem of incidence does not appear to be entirely one of histogenesis. Myoethelium in human tumours is found, in my experience, mainly in benign tumours, both fibroadenomas and papillomas, which if clinically apparent are frequently removed in the earlier ages. Even if we could assume that bone and cartilage are the product of myoethelial activity in these human mammary tissues, the likelihood of this metaplasia is small. Gross (1887) found only 4 examples in 156 cases in the literature and had seen only 1 case himself; most later cases were reported as single examples. In large tumours (see cases 34, 35 and 37) the possibility of tracing the genesis of bone or cartilage from myoethelium would be obliterated.

In the early stages of myoethelial proliferation comparable appearances were occasionally found in human and canine tumours as shown in figs. 356, 357, 360 & 361 (human) and fig. 376 (canine).

Osteoblasts associated with osteoid tissue were also seen in both human (fig. 374) and canine cases (fig. 331) with myoethelial activity, but my material shows no further development in human cases towards bone or cartilage formation. Myoethelium appeared to become or to be incorporated into the underlying stroma (figs. 359 & 361) or to form a palisaded supporting tissue with no evidence of bone or cartilage (fig. 365). It may largely replace glandular structure by forming loose sheets of irregularly rounded and polygonal cells (figs. 367 & 369) or may be found associated with pleomorphic fibrosarcoma (fig. 375) which shows no bony or cartilaginous features and also no evidence of transition from the benign to the malignant areas.

The later course of myoethelial activity in canine mammary tumours appears different and also progressive, or at least to give evidence of definite bone and cartilage when examined. The glandular structures are eliminated by a myomatous-looking reticular meshwork of myoethelium (figs. 377 & 379) or by intracanalicular polypoidal myoethelial proliferation which eventually forms a fibrosarcomatous tumour (fig. 390) with little or no epithelial structures. The course of pericanalicular growth is very similar. Cartilage may be calcified and form with early bone and marrow a picture very like foetal growth (fig. 383), a stage I have not seen in human tissue. Cartilage also forms directly from myoethelium, a phase also not found in the human material personally examined. My available human material does not admit of further comparison or explanation.

The canine malignant lipomyxomatous tumours shown in figs. 385 & 386 are the only examples of these neoplasms in the bitch which I have encountered.

Professor Cotchin is of the opinion that much light could be thrown on the nature and function of myoethelium by electron microscopy. (1968).

Human Mammary Tissue with "Myoepithelium" Figs. 355 - 375

Unstriated muscle in the breast is limited normally to the walls of arterioles and venules. If proliferating pathologically, it usually needs differential staining to distinguish it from fibrous or neural tissue. In benign fibro-epithelial tumours of the breast, it is sometimes found encircling glandular structures and derived from the walls of adjacent blood vessels, as in fig. 355, a fibroadenoma of combined peri- and intra-canalicular type. In these tumours broad strands of unstriated muscle may also be found in and between the larger polypoid formations.

Myoepithelium is a different tissue and its nature and histogenesis are still uncertain. It has received little attention in human mammary studies, Biggs' article (1947) on "The myoepithelium in certain tumours of the Breast" being the only reference in the J. Path. Bact. from 1892 to 1965, but Bonser et al. have discussed the subject at some length in their book, "Human and experimental mammary tumours" (1961). Myoepithelium occurs much more frequently in canine than in human tumours and has been described and discussed at length in the veterinary literature of various countries. It is of interest therefore to compare its structure in human and in canine material in the following illustrations and discuss briefly the reasons for this difference in incidence.

The following illustrations are from human material.

- Figs. 356 and 357. The same area of a large fibroadenoma with much myoepithelium proliferating between the lining epithelium and the basement membrane.
- Fig. 358. In the cellular areas of a cystic fibroadenoma, myoepithelium is also a distinct, fairly continuous subepithelial layer.
- Fig. 359. Same tissue, where the myoepithelium appears to merge (lower right) with the active mitotic underlying supporting tissue.
- Fig. 360. Myoepithelium is sometimes very easily identified in benign papillomas.
- Fig. 361. Same, showing the subepithelial layer with some irregular proliferation.
- Fig. 362. An enlarged cystic breast, female child aged 19 months, with papillary growth in the fluid of dilated ducts.

- Fig. 363. Same, showing apparent myoepithelium as the "stromal" tissue.
- Fig. 364. Some proliferation of the myoepithelial layer in a cystic duct of a papillomatosis.
- Fig. 365. Occasional palisading in the supporting tissue suggests derivation from the subepithelial layer and emphasizes its smooth muscle character.
- Fig. 366. Continued proliferation of the myoepithelium in a benign glandular tumour may cause atrophy of the epithelial layer and gradually replace it.
- Fig. 367. A similar replacement of glandular structure in the breast is shown in this cystic fibroadenoma in areas now a "myoadenoma".
- Fig. 368. Same, stained by reticulin, showing the lobulated, defined periphery.
- Fig. 369. Same, at higher magnification.
This is the only example of a "myoadenoma" personally encountered.
- Fig. 370. Part of a parotid gland adenoma becoming purely myoepithelial with 2 remaining ducts.
- Fig. 371. Small fibroadenoma, with early osteoid in centre of field?
- Fig. 372. A very large, rapidly growing tumour, diagnosed elsewhere as myoadenoma. Proliferating myoepithelium near duct, top left, and early osteoid? lower field.
- Fig. 373. Same tumour with proliferating myoepithelium round central duct and early osteoid?
- Fig. 374. A cystic fibroadenoma with active myoepithelium and early osteoblasts round osteoid.
- Fig. 375. Same tumour, with monstrous nuclei and mitotic figures.

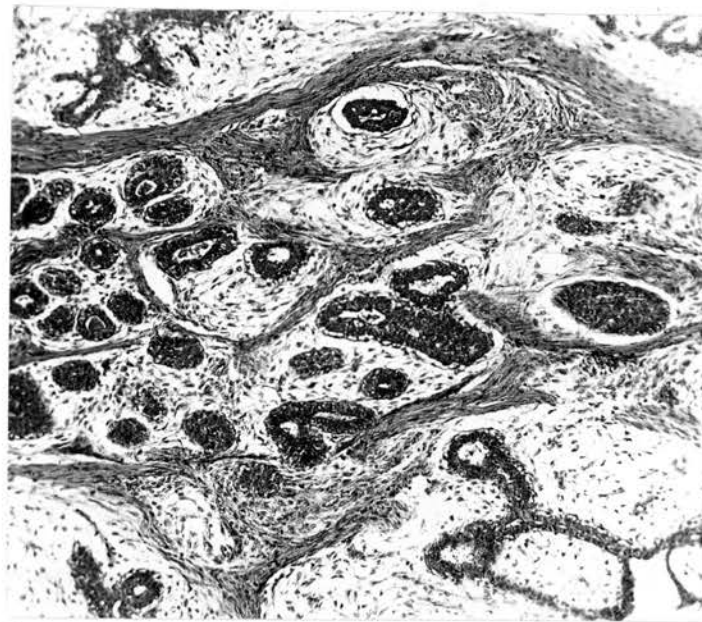


Fig. 355.

x80.

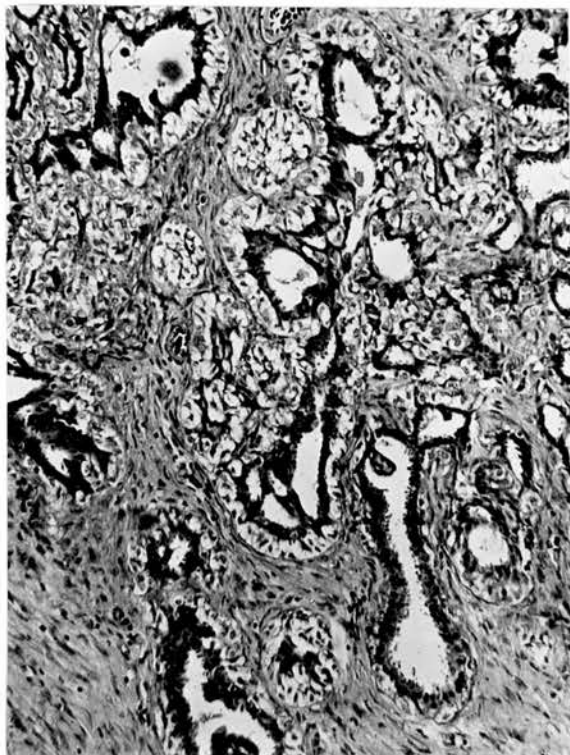


Fig. 356

x130

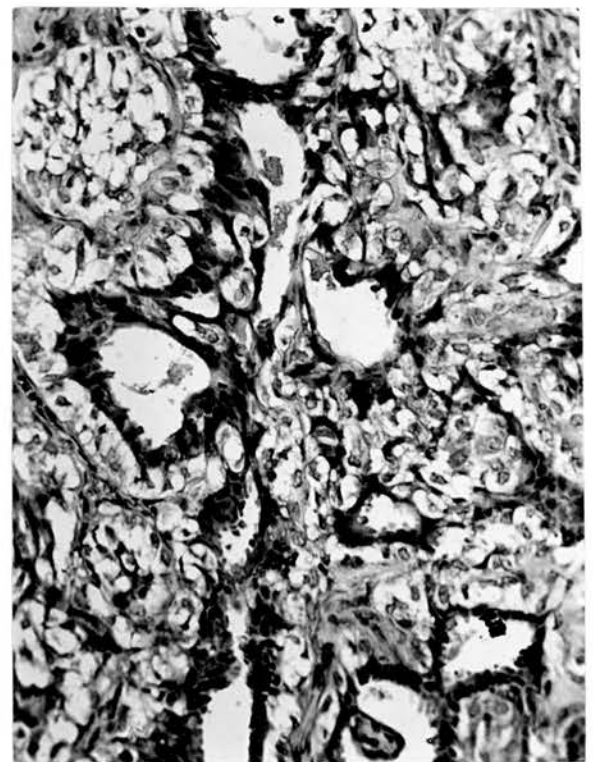


Fig. 357.

x250

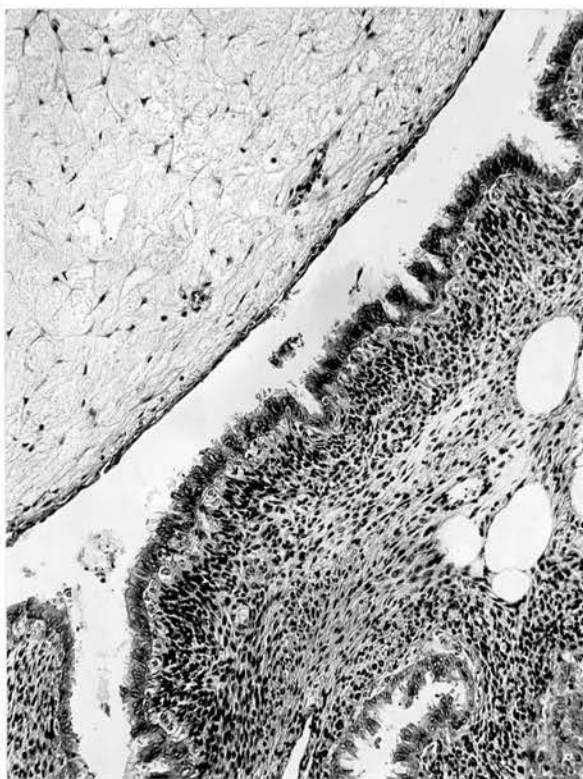


Fig. 358.

×100.

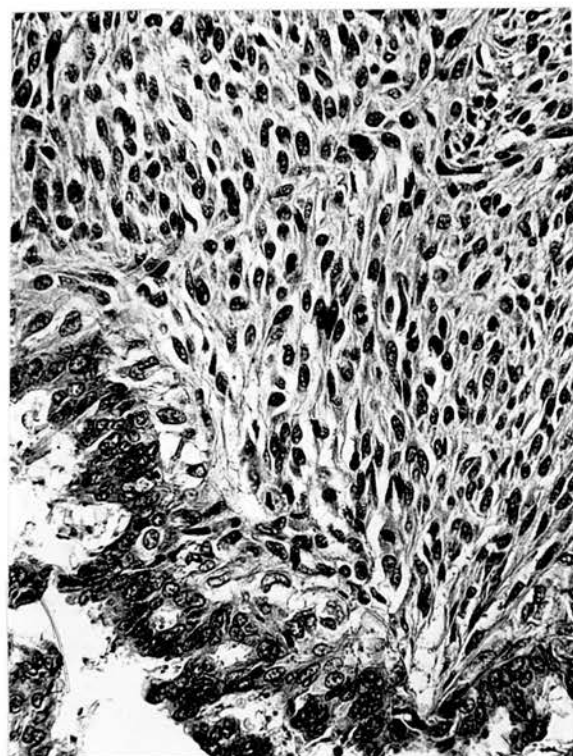


Fig. 359.

×300.

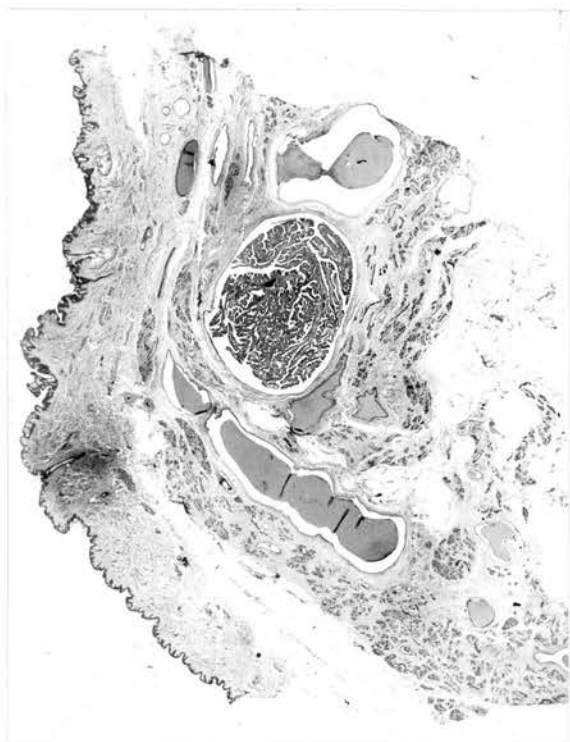


Fig. 360.

×9.

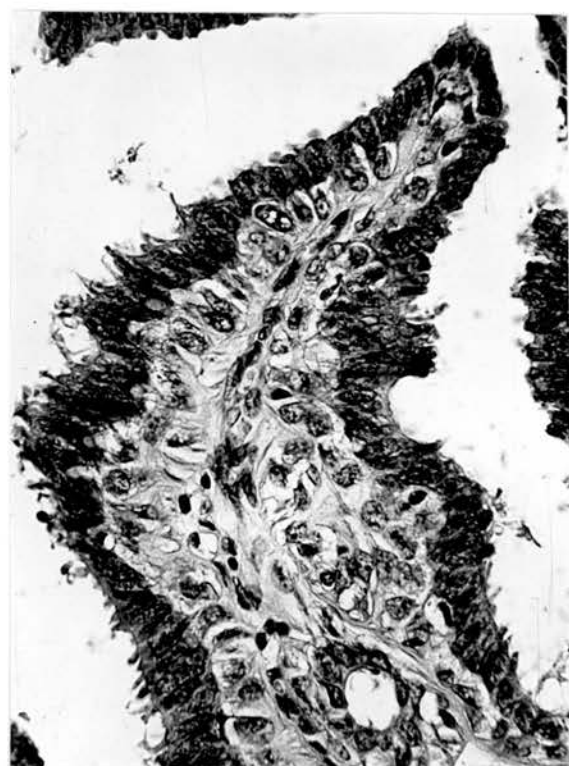


Fig. 361.

×375.



Fig. 362.

x2.

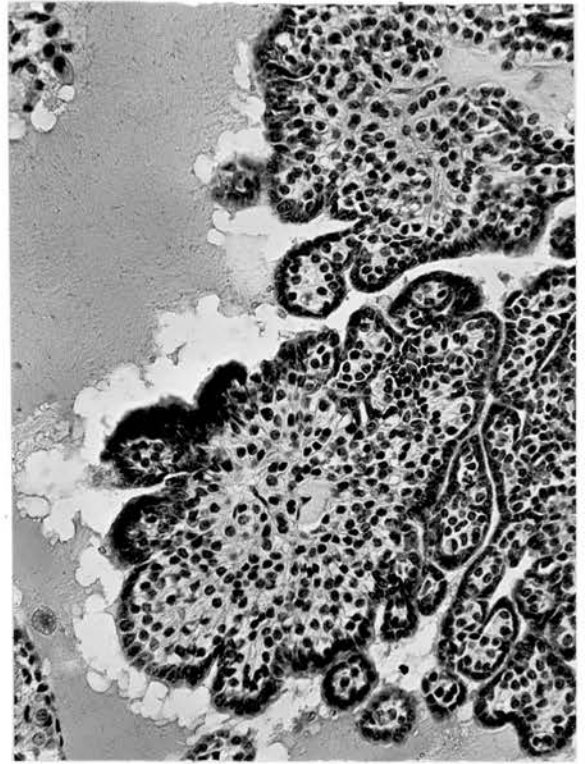


Fig. 363.

x250

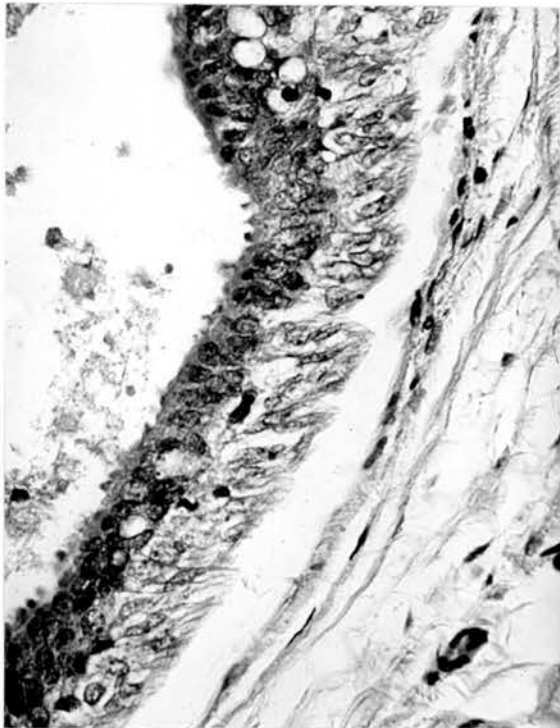


Fig. 364.

x450

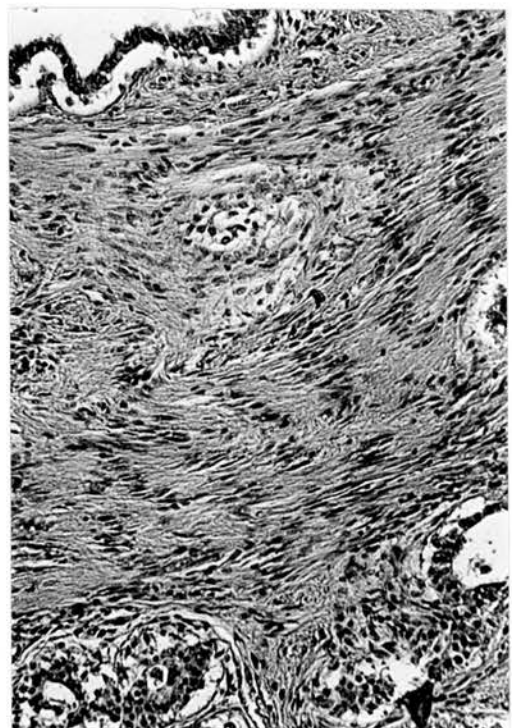


Fig. 365.

x150

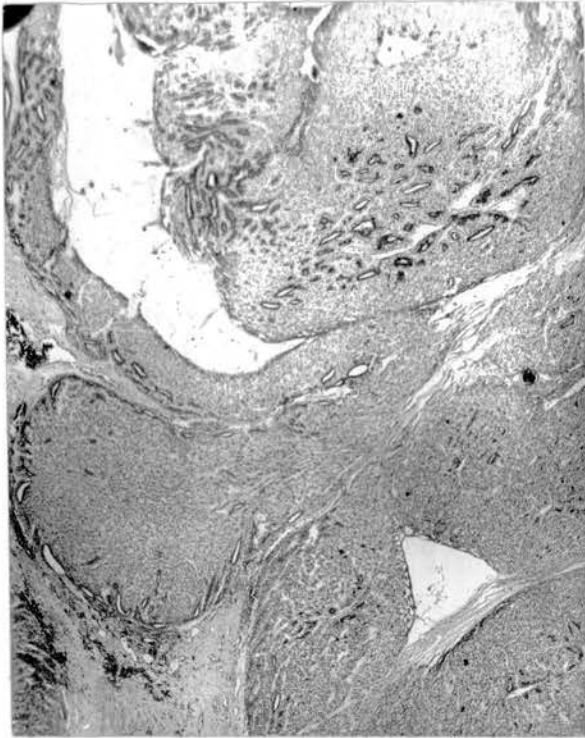


Fig. 366.

x 20.

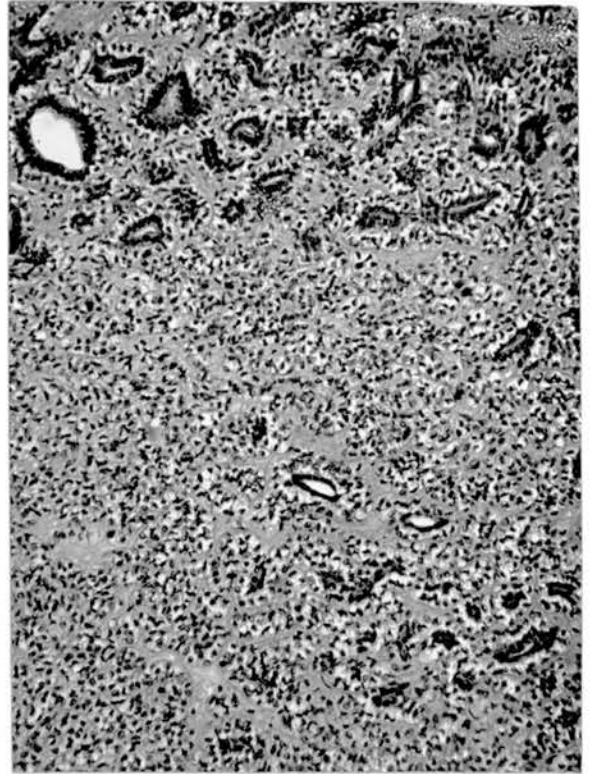


Fig. 367.

x 100.

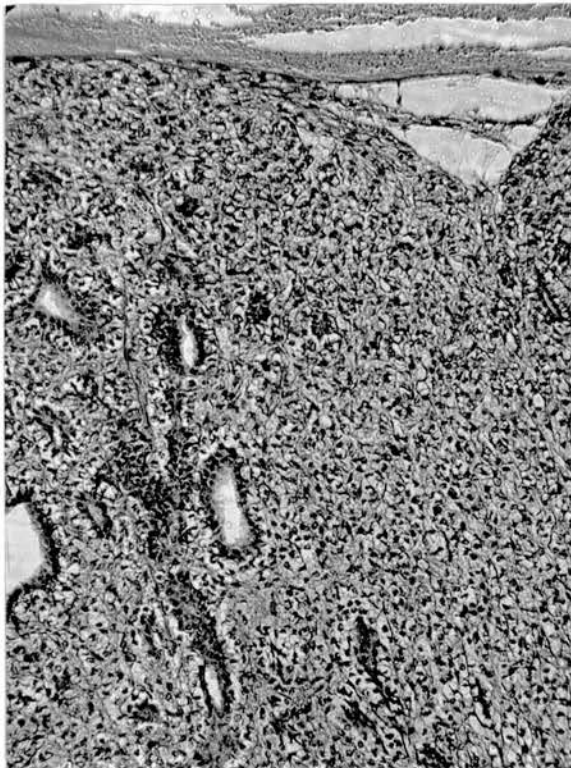


Fig. 368.

x 100

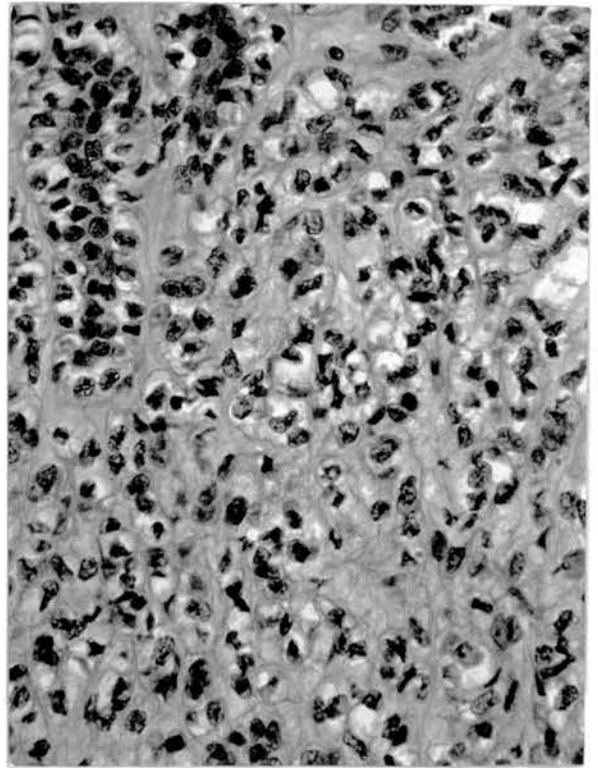


Fig. 369.

x 425.



Fig. 370 (Salivary Gland). x225



Fig. 371. x150.

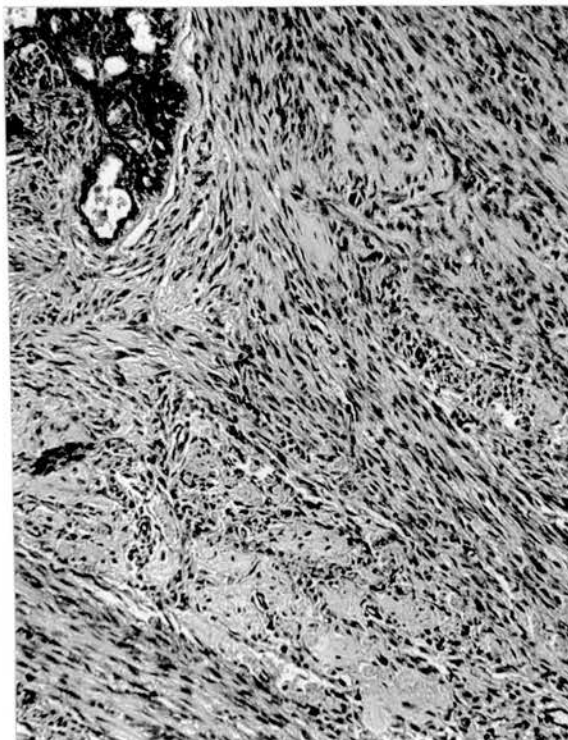


Fig. 372. x110.

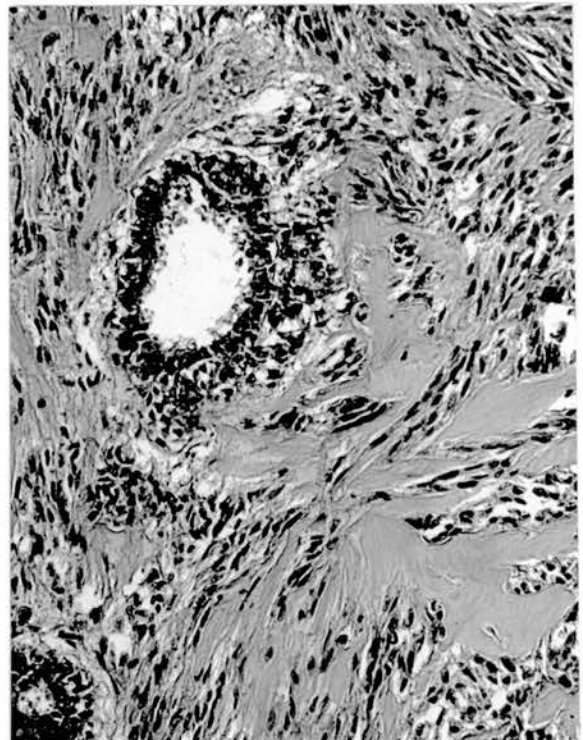


Fig. 373. x170.

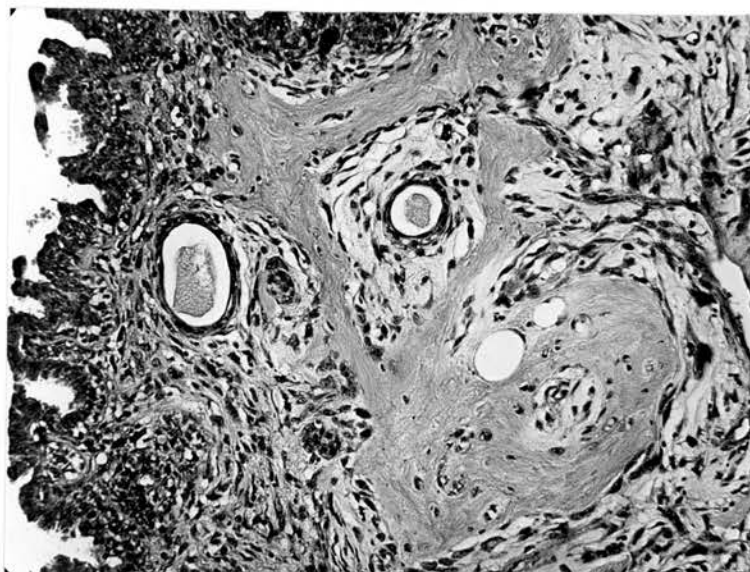


Fig. 374.

× 120.

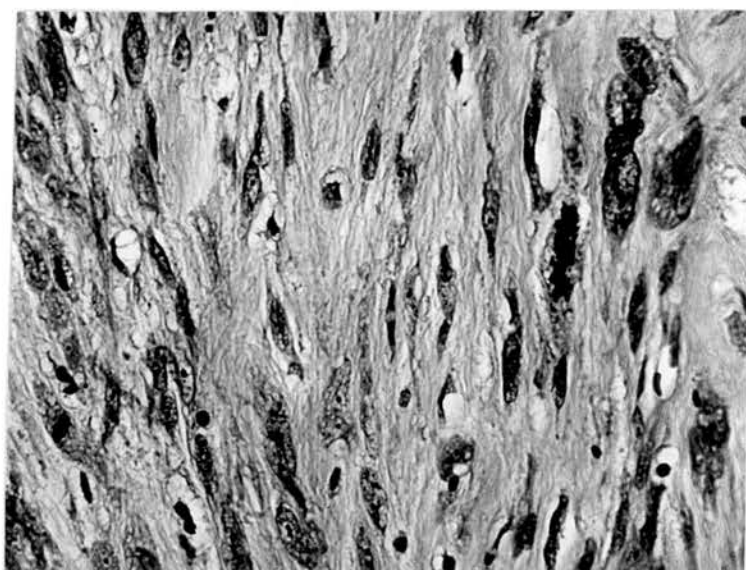


Fig. 375.

× 325.

Canine Mammary Tissue with "Myoepithelium" Figs. 376 - 383.

- Fig. 376. Mammary glands showing myoepithelium inside the hyalinized basement membrane and some early disintegration of the lining epithelium, similar to human appearances in fig. 356.
- Fig. 377. Same tissue, glands with more compressed epithelium and myoepithelium passing into a loose sheet of long, thin spindle cells.
- Fig. 378. Part of a cystic papillary carcinoma; glands here show irregular myoepithelial proliferation, with basement membrane being lost in osteoid (middle field).
- Fig. 379. Same area, showing myoepithelium with benign and malignant glands. Compare fig. 374 (human).
- Fig. 380. An intracanalicular fibroadenomatous pattern with polypoid masses of predominant myoepithelial proliferation, not yet destroying the covering epithelium.
- Fig. 381. Myoepithelium below epithelium, forming bone only, partly outlined by osteoblasts.
- Fig. 382. Calcifying osteoid and a few osteoclasts in a polypoid myoepithelial area.
- Fig. 383. Osteochondroma with calcifying cartilage and bone with osteoblasts and marrow.

Other Canine Mammary Sarcoma Types.

- Fig. 384. Lipomyxosarcoma with some fibrous tissue; very cellular fat is the predominant component.
- Fig. 385. Cellular fat with mitotic activity. (Compare figs. 36 & 37).
- Fig. 386. Pools of mucus with scattered fat cells in a cellular malignant fat background, as in human myxoliposarcoma. (Compare fig. 187).
- Fig. 387. Haemangiopericytoma, metastasis in liver from a primary mammary tumour of bitch. Very similar to the tumour found in humans, primary and metastatic. (Compare figs. 202 & 203). Some liver cells are surviving on left edge of area.
- Fig. 388. Mammary sarcoma of mouse, with mild pleomorphism but no special features.

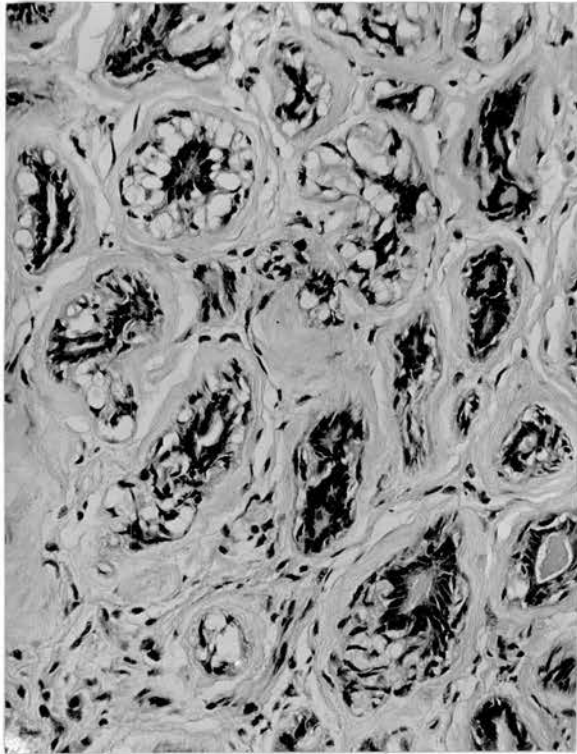


Fig. 376.

x225.

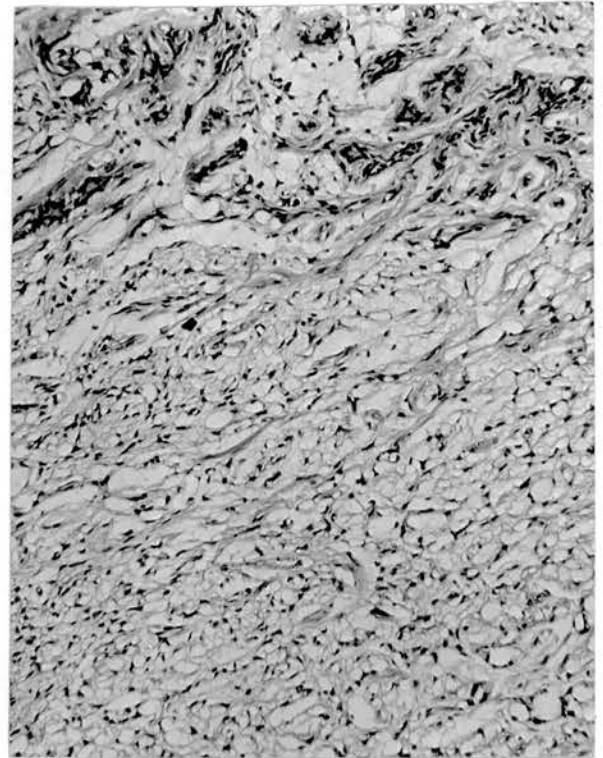


Fig. 377.

x130

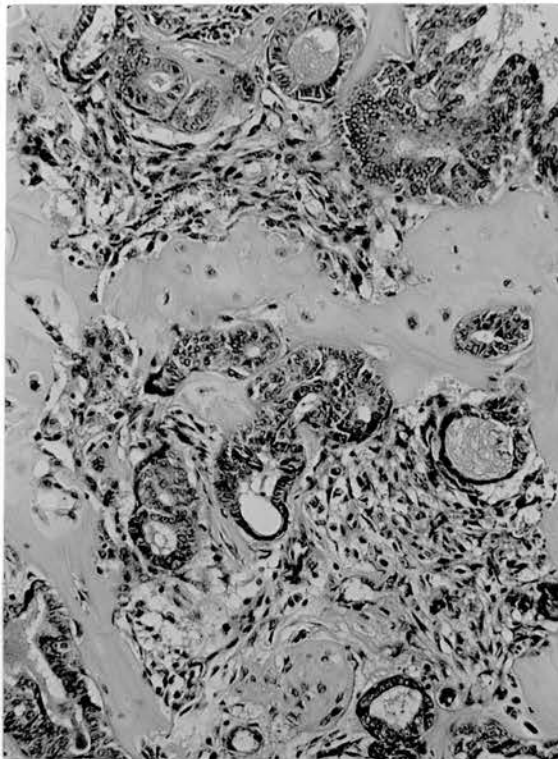


Fig. 378

x130.

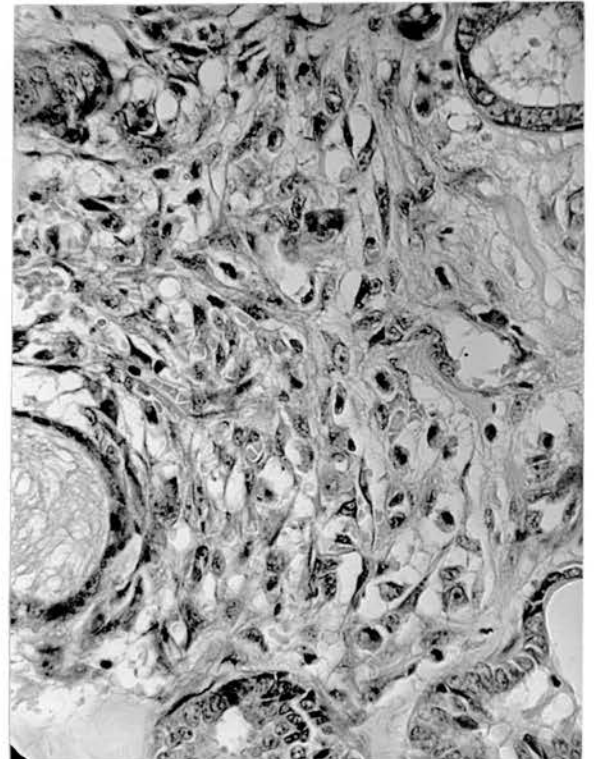


Fig. 379.

x325.

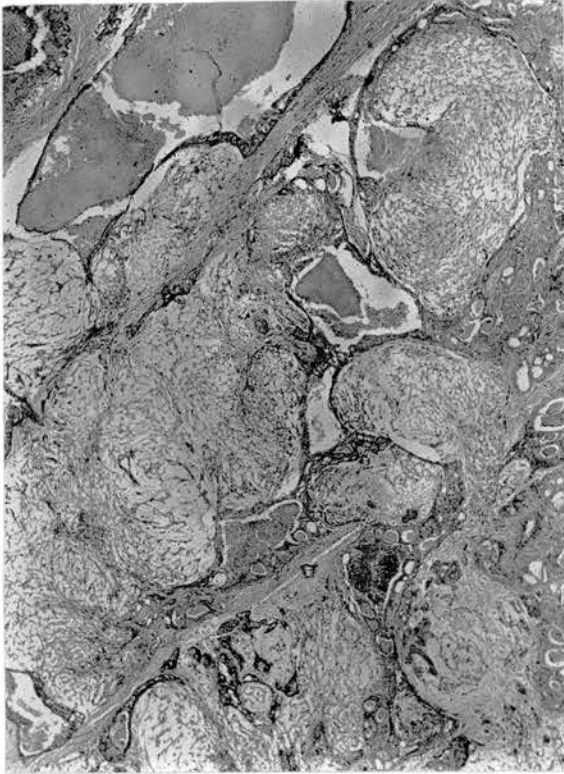


Fig. 380.

×25.

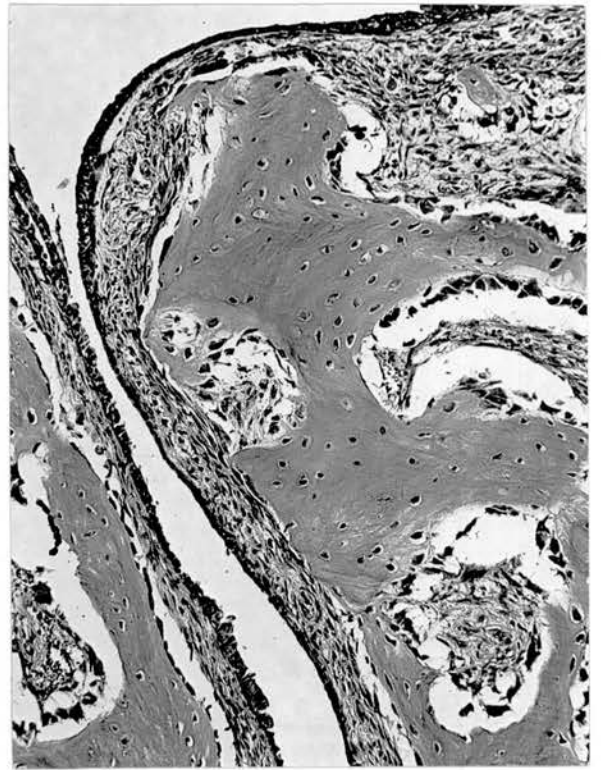


Fig. 381.

×100

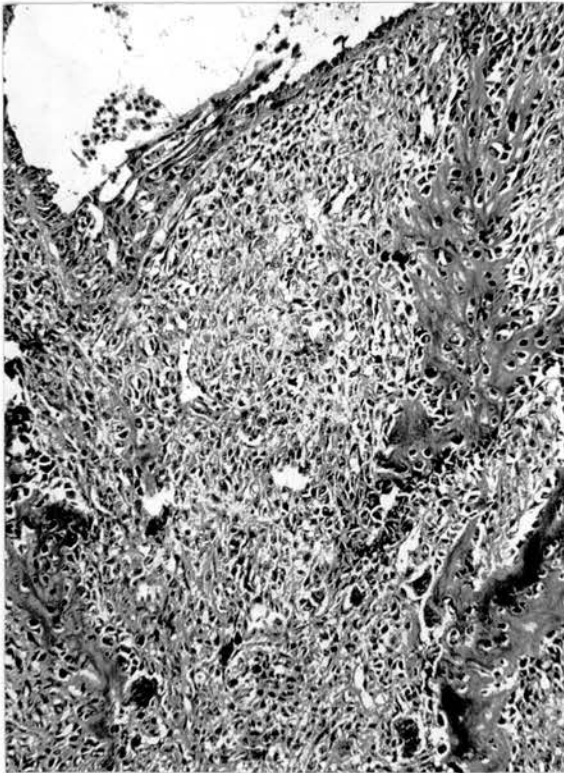


Fig. 382.

×100.

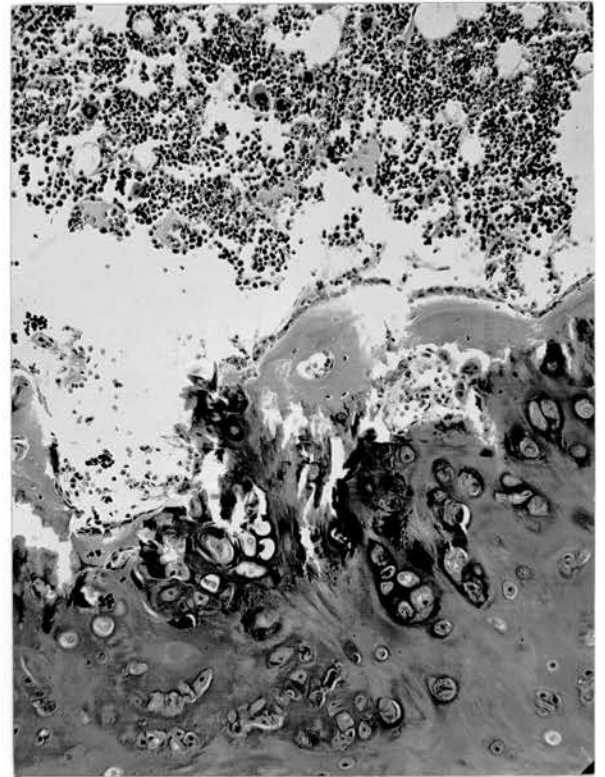


Fig. 383.

×100 .

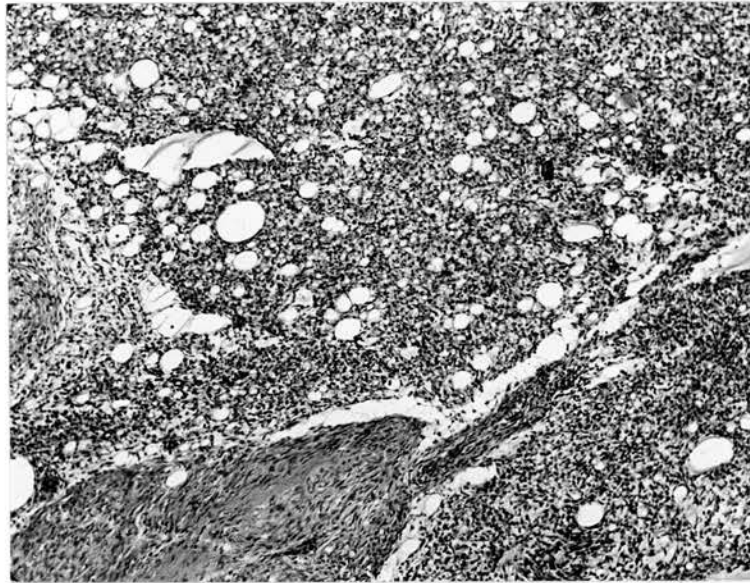


Fig. 384.

x 75.

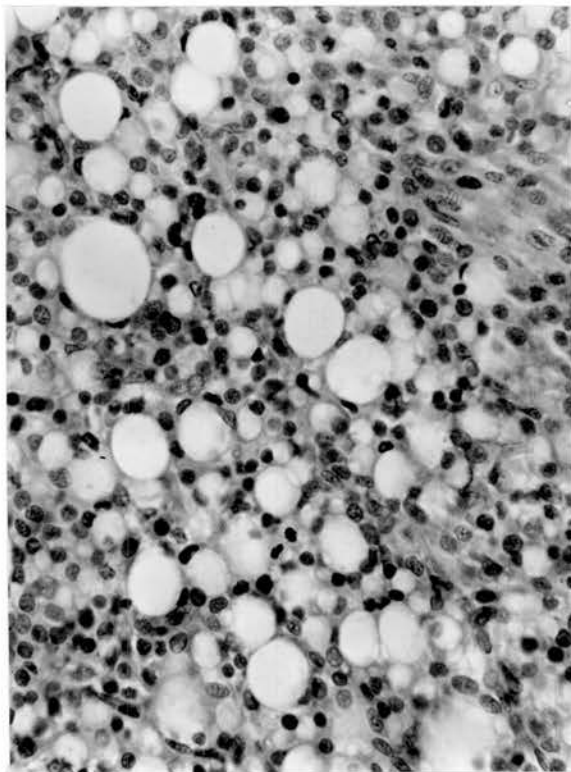


Fig. 385.

x 400.

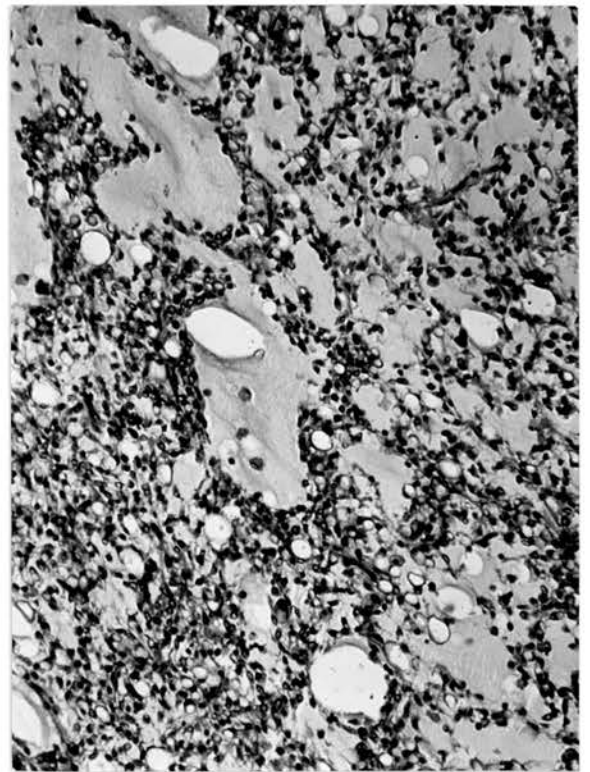


Fig. 386.

x 150.

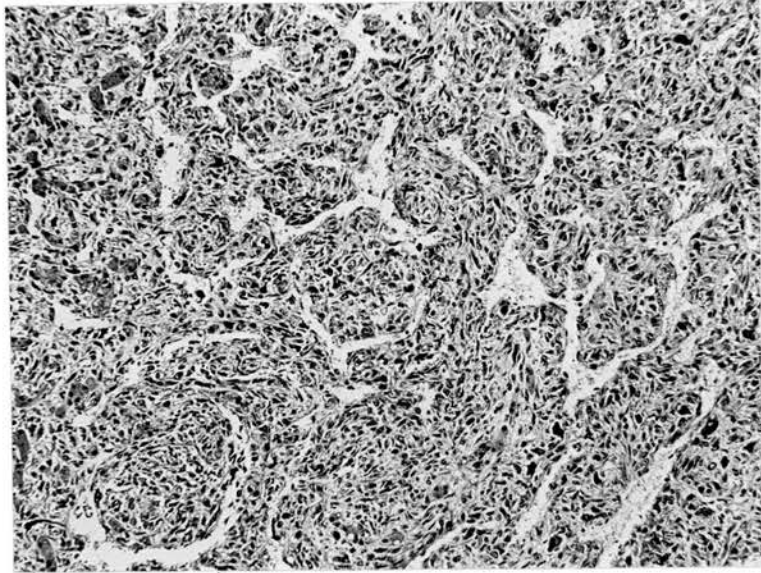


Fig. 387.

× 100

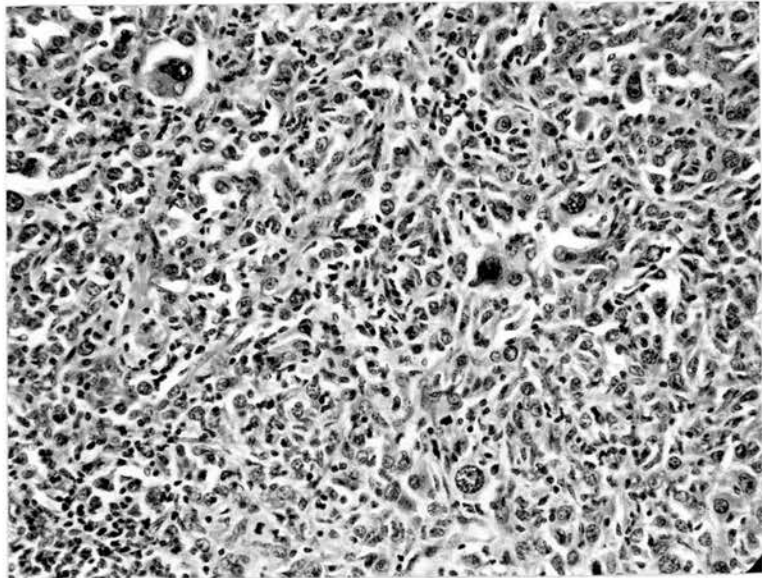


Fig. 388.

× 250

Conclusion

"Uncommon conditions are an important source of information in extending the periphery of our field of knowledge".

- King (1950).

In a histological study it is not the first aim of the investigator to formulate theories but to observe and record facts.

This series of cases has illustrated not only the histological character and the variants of these tumours but has indicated in many, the genesis. It becomes therefore possible to regard the presence of a sarcoma as the end product of a long continuing process of cell proliferation. There is no clear evidence of why the transition from innocence to malignancy should occur but in at least one small group of the cases pregnancy may have played a significant role. If such a speculation should prove correct the comparison to the behaviour of mammary carcinoma in response to pregnancy is striking.

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